CASE REPORT
SUPPRESSION OF SYMPTOMS OF ALCOHOL DEPENDENCE AND CRAVING USING HIGH-DOSE BACLOFEN
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Abstract — Aims: To further test whether the baclofen-induced suppression of motivation to consume alcohol in animals could be transposed to humans. Methods: A patient who had neither tolerated nor benefited from other alcohol treatment modalities was put on trial with baclofen on a dosage up to 140 mg/day. Results: The patient reported dramatic reduction in cravings for and preoccupation with alcohol. Conclusions: High-dose baclofen therapy was associated with complete and prolonged suppression of symptoms and consequences of alcohol-dependence.

INTRODUCTION
In the past decade, scientists have made important progress toward understanding the neurobiology underlying drug and alcohol addiction. Consequent development of new pharmacotherapies has been shown to substantially improve the outcomes of patients treated with standard alcohol therapies (individual and/or group supportive psychotherapy, cognitive behavioral therapy; 12-step programs). FDA approval has been granted for three agents thus far. Listed in order of FDA approval dates, these are disulfiram, oral naltrexone, acamprosate, and recently an extended release (30 day) injectable suspension of naltrexone. The latter, having just been released, has not yet had wide spread use in clinical settings. Although Garbutt et al. (2005) did associate injectable naltrexone with a lower number of heavy drinking days per month in alcohol-dependent individuals, the number did not continue to diminish over the long duration of the trial. This may be because naltrexone has never been shown to completely eliminate craving for alcohol. Craving has been shown in some studies to predict drinking behavior (Bottlender and Soyka, 2004). Craving remains, nonetheless, an ill-defined concept. Clinical assessment of craving remains of unclear value. Reduction of heavy drinking days has been previously established in randomized trials with the oral naltrexone (Balldin et al., 2003), topiramate (Johnson et al., 2003), baclofen dosed 10 mg t.i.d. (Addolorato et al., 2002), and in an open-label trial of acamprosate (Soyka and Chick, 2003).

In validated animal models for craving for alcohol (Koob, 2000), one of these agents, baclofen, which is a GABA(β) receptor agonist, has been shown in high dose to completely suppress motivation to consume alcohol. The suppressing effect is dose-dependent (Colombo et al., 2003). Acamprosate has also been shown to reduce self-administration of alcohol in alcohol-prefering rats (Cowan et al., 2005). Naltrexone reduced but do not eliminate self-administration of alcohol. Animal data are not available for topiramate (Ameisen, 2005a).

Anxiety disorders (Breslow et al., 1989; Drake et al., 2003) and anxiety associated with affective disorders (Addolorato et al., 2002a, b, 2006) have been shown to be ameliorated by baclofen. Clinically significant anxiety is commonly comorbid with alcohol dependence (Grant et al., 2004). Efficacy on anxiety has not been shown for other agents used for alcohol dependence (Ameisen, 2005b). Thus it appears, upon review of the literature, that baclofen is the only agent capable of completely suppressing cravings, while alleviating comorbid anxiety.

The data presented thus far was previously reported in a letter to the editor of Journal of the American Medical Association (Ameisen, 2005a) and in a case study authored by Olivier Ameisen, MD, who used himself as the subject of study (Ameisen, 2005b). Dr. Ameisen had previously tried recommended dosages of disulfiram, oral naltrexone, acamprosate, and topiramate and had had extended periods of abstinence utilizing CBT and extensive involvement in alcoholics anonymous (AA). He nevertheless persisted to have alcohol cravings and anxiety symptoms, which had predated his alcohol dependence, despite trials of buspirone, selective serotonin reuptake inhibitors, valproate and carbamazepine. Hypothesizing that the dose-dependent suppression of alcohol consumption (3 mg/kg body wt) in animals could be transposed in humans, he subjected himself to a trial. He self-prescribed baclofen up to 270 mg/day (3.6 mg/kg body wt) during the first 37 days and experienced, for the first time in his alcoholic life, the absence of craving for alcohol. Indeed, he reported a state of complete and persistent indifference to alcohol, along with substantial reduction of anxiety, for a duration of 9 months at the time of his report. For reasons of somnolence, he subsequently reduced his dosage to 120 mg/day and used extra 40 mg p.r.n. stressful situations. The somnolence abated and he never experienced muscle weakness or other side-effects. Blood tests remained within normal limits.

PATIENT AND METHODS
Mr. A is a 59-year-old married successful businessman who frequently presides over national conventions and speaks before hundreds of people. He enjoys a stable home life, does not smoke, has no other chronic medical illnesses, and exercises regularly. He sought my services as an addiction

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psychiatrist in May 2005 despite having a beneficial ongoing relationship with both a psychologist and a psychiatrist for the management of depression and anxiety. He had been given a diagnosis of major depressive disorder. His symptoms had responded to paroxetine over the previous 2–3 years. Prior to taking paroxetine he had had trials of fluoxetine, citalopram, and sertraline which he considered to have been tainted by his heavier alcohol consumption at the time. He spontaneously identified himself as an alcoholic and presented a strong family history of the same. He presented with a strong distaste for AA meetings, which he had tried, and refused to consider returning. He was not interested in a recommendation for outpatient chemical dependency programming. In counseling sessions he was advised to pursue abstinence from alcohol.

His ardent desire, however, was to be able to control his drinking so as to not have it continue, in its unpredictable fashion, to embarrass and/or episodically incapacitate him in his professional endeavors. Toward that end, he had already completed the Drinkwise program offered through the University of Michigan. This program utilizes CBT techniques to assist those with an alcohol abuse diagnosis to be able to drink in a controlled fashion, if they so choose. It did not work for him, which appropriately led him to his own conclusion that he had alcohol dependence rather than alcohol abuse.

Through his other psychiatrist he had already taken oral naltrexone. A dosage of 100 mg/day had initially been necessary before he noticed any attenuation of his alcohol cravings. This was short-lived, however, and by the time he presented to me he was taking 150 mg/day with no apparent benefit. He was still consuming an average of 35 drinks distributed over a week and up to 12 drinks per occasion. He remained concerned about the potential damage such drinking might do to his health, professional and home life. I recommended he continue naltrexone at 150 mg/day and added acamprosate 2 g/day. After 1 month, that did not reduce his craving or drinking so I offered a trial of topiramate in its place. Topiramate, similarly, offered no benefit and was associated with word-finding difficulties, a side-effect he could not abide.

At this juncture, September 2005, a trial of baclofen was agreed upon. Scales to evaluate craving and laboratory parameters were not used. Over the first month he gradually increased his dosage to 100 mg/day, taken on a t.i.d schedule, and reported a completely satisfactory response. He felt that drinking was now “an alien world” to him. On occasion, when stressed, he increased his dosage to 140 mg/day. He experienced only mild relaxation, not sedation, as a side-effect. This benefit did not abate, as had been his experience with naltrexone, and he continued to report baclofen as “my miracle drug.” If he chose to drink his consumption was never more than 12 per week, or 3 per occasion, and his sense of euphoria from that was dulled. With the guidance of his other psychiatrist he discontinued the paroxetine, experienced return of depression and anxiety, had a brief unsuccessful trial on effexor XR 75 mg, and returned to paroxetine.

**DISCUSSION**

Having worked with chemically dependent individuals struggling for recovery for over 20 years, I am a supporter of AA and Narcotics Anonymous (NA) and believe connection with those organizations to be the most likely route toward quality recovery. With or without such a connection, however, I have repeatedly been faced with the patient who, despite his or her apparent best efforts, has not been successful at resisting the impulse to relapse, even when I believe I have successfully treated psychiatric comorbidity. I have experienced such patients benefiting from either oral naltrexone, acamprosate, or the combination of both. I make disulfiram available to patients whom I believe it will help, but do not rely upon it to reduce the phenomenon of craving. I have yet to treat anyone with injectable naltrexone.

Mr. A is an individual whom I believe represents a very large number of patients who do not experience a satisfactory anti-craving response to either the current FDA-approved medications for alcohol dependence or to topiramate. My report is that he has experienced a satisfactory response to high-dose baclofen that has been sustained over ten months without significant side-effect. Tolerance has not developed, whereas it had with oral naltrexone. Tolerance to baclofen has uncommonly been reported only after years of intrathecal use for severe spasticity (Nielsen et al., 2002). In contrast with Dr. Ameisen’s experience, use of a selective serotonin reuptake inhibitor (SSRI, paroxetine) did appear to be necessary as baclofen by itself did not satisfactorily reduce Mr. A’s anxiety or depression.

Being a case study, this report is obviously limited. Placebo response is a possibility. If that is the case, however, there is no apparent explanation for why it did not appear in trials of either naltrexone or acamprosate, alone or in combination, or with topiramate. Given the nearly four decades of use of high-dose baclofen for the long-term comfort care of patients with muscular spasticity from various neurological conditions (spinal injuries, multiple sclerosis), and the absence of report of serious or irreversible adverse effect, baclofen may be a safe, effective and well-tolerated adjunct to our treatment efforts with this population. Hypotension, changes in glucose control in diabetics, sedation and changes in seizure control are potential side-effects. Randomized trials of high-dose baclofen should be conducted to test elimination of alcohol craving and its potential consequences.

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**REFERENCES**


Ameisen, O. (2005b) Complete and prolonged suppression of symptoms and consequences of alcohol-dependence using...


