

CASE REPORT

COMPLETE AND PROLONGED SUPPRESSION OF SYMPTOMS AND CONSEQUENCES OF ALCOHOL-DEPENDENCE USING HIGH-DOSE BACLOFEN: A SELF-CASE REPORT OF A PHYSICIAN

OLIVIER AMEISEN*

23 rue du Départ BP37, 75014 Paris, France

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Abstract — **Aims:** To test whether the dose-dependent motivation-suppressing effect of baclofen in animals could be transposed to humans, and suppress craving and sustain abstinence. **Methods:** Neurologists safely use up to 300 mg/day (10 times the dosage currently used for alcohol dependence) of high-dose oral baclofen, to control spasticity, in order to avoid invasive therapy. I am a physician with alcohol dependence and comorbid anxiety. I self-prescribed high-dose baclofen, starting at 30 mg/day, with 20 mg increments every third day and an (optional) additional 20–40 mg/day for cravings. **Results:** Cravings became easier to combat. After reaching the craving-suppression dose of 270 mg/day (3.6 mg/kg) after 5 weeks, I became and have remained free of alcohol dependence symptoms effortlessly for the ninth consecutive month. Anxiety is well controlled. Somnolence disappeared with a dosage reduction to 120 mg/day, now used for the eighth consecutive month. **Conclusions:** High-dose baclofen induced complete and prolonged suppression of symptoms and consequences of alcohol dependence, and relieved anxiety. This model, integrating cure and well-being, should be tested in randomized trials, under medical surveillance. It offers a new concept: medication-induced, dose-dependent, complete and prolonged suppression of substance-dependence symptoms with alleviation of comorbid anxiety.

INTRODUCTION

Alcohol dependence symptoms (craving, preoccupation) are defined as chronic (Morse and Flavin, 1992), and current therapeutic approaches are based on the idea that such symptoms can be attenuated but not suppressed. Therefore, medical trials set abstinence with lower-grade craving as the declared goal (Addolorato *et al.*, 2000, 2002a; Pelc *et al.*, 2002; Froehlich *et al.*, 2003; Johnson *et al.*, 2003, 2004).

I am a physician diagnosed with alcohol dependence and comorbid anxiety disorder according to the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) (American Psychiatric Association, 1994). I had been hospitalized for acute withdrawal seizures. Anxiety disorder had long preceded addiction.

I had tried recommended dosages of medications proposed for promotion of abstinence and reduction of craving (see Patient and Methods). I had achieved prolonged abstinence with and without medications. But I had always experienced cravings and preoccupation with alcohol, and achieving abstinence in such conditions required daily planning as well as constant and full attention.

Baclofen is a potent gamma-aminobutyric acid (GABA_B) receptor agonist clinically used to control spasticity (Davidoff, 1985):

- (i) In alcohol-dependent patients, low-dose baclofen at 30 mg/day (~0.5 mg/kg) was shown to be effective in promoting abstinence, reducing alcohol craving and consumption, with no limiting side-effects (Addolorato *et al.*, 2000, 2002a,b).
- (ii) In rats, at doses up to 10 times higher (5 mg/kg), baclofen suppresses cocaine self-administration, motivation to

consume alcohol and attenuates self-administration of cocaine, alcohol, heroin, nicotine and D-amphetamine (Roberts and Andrews, 1997; Shoaib *et al.*, 1998; Xi and Stein, 1999; Colombo *et al.*, 2000, 2003; Fattore *et al.*, 2002; Brebner *et al.*, 2004). Effects are dose-dependent for each substance. For alcohol, up to 3 mg/kg are required.

- (iii) In multiple sclerosis, neurologists safely use long-term high-dose oral baclofen (270 mg/day), to control spasticity, in order to protect patients from risks of invasive intrathecal therapy (Smith *et al.*, 1991). Given the safety record of baclofen since 1967, neurologists with experience in spasticity do not hesitate to use up to 300 mg/day of baclofen, as long as somnolence and/or muscular weakness do not limit treatment (John Schaefer, Cornell University Medical College, personal communication). In the highest recorded baclofen overdose (acute ingestion of 2 g), the patient survived (Gerkin *et al.*, 1986).

I postulated the notion that dose-dependent suppressing effects could be transposed to humans and that by using baclofen in dose ranges used in animal studies, one might reach a critical dose at which craving and motivation to drink alcohol might be suppressed in alcoholics, thus substantially reducing relapse risk.

Baclofen has also been used successfully in anxiety disorders (Breslow *et al.*, 1989; Drake *et al.*, 2003), and was shown to be effective in ameliorating some affective disturbances in alcoholic patients, including anxiety and depression (Krupitsky *et al.*, 1993; Addolorato *et al.*, 2002a,b). Anxiety is an overwhelmingly prevalent comorbidity of alcoholism (Grant *et al.*, 2004), and efficacy on anxiety has not been shown for other agents used for alcohol dependence (disulfiram, naltrexone, acamprosate or topiramate). I had used baclofen for >1 year (2002–2003) to

*Correspondence: Tel: +33 675599914. E-mail: oameisen@noos.fr

reduce anxiety. I had progressively increased the dosage to 180 mg/day, which improved personal and general well-being considerably, but did not suppress cravings and alcohol relapses. Being unaware then that higher dosages were safe, I had not exceeded 180 mg/day.

By analysing the literature, I subsequently realized that baclofen was the only monotherapy that could, in theory, completely suppress cravings, while alleviating comorbid anxiety simultaneously. Although my doctors remained unconvinced, I decided to self-prescribe high-dose baclofen, choosing 300 mg/day (4 mg/kg) as the maximal daily dosage, as long as side-effects were not limiting.

PATIENT AND METHODS

On January 9, 2004, I was a 50-year-old white French-American male physician with alcohol dependence and comorbid pre-existing anxiety disorder. Since 1997, there had been numerous emergency hospitalizations, emergency room visits, detoxifications, years of inpatient and outpatient rehabilitation treatments. I bear no medical sequelae. On a typical drinking day, I consumed ~750 ml of Scotch. Treatment had included 500 mg/day of disulfiram (I did drink while taking it). Thereafter, I had consecutively and for each medication been on 12–18 months of naltrexone (50 mg/day), acamprosate (2 g/day) and baclofen (180 mg/day). I have subsequently been on topiramate (300 mg/day) for 3 months. Naltrexone and acamprosate had been discontinued because there had been no perceptible effects on cravings or relapse reduction. During this time, I benefited from cognitive behavioural therapy (CBT) and Alcoholics Anonymous (AA) meetings. I attended around two AA meetings a day, making roughly 700 meetings a year, over a period of 7 years.

Anxiety was refractory to buspirone, specific serotonin re-uptake inhibitors, valproate and carbamazepine. In May 2003, hoping to achieve complete abstinence, I tapered baclofen and self-prescribed topiramate following an outlined schedule (Johnson *et al.*, 2003). I continued with 300 mg/day of topiramate for 3 months despite side-effects (memory, speech). Topiramate had no efficacy in reducing anxiety and I suffered a severe relapse.

On January 9, 2004, day 1 of post-relapse abstinence, I started oral baclofen monotherapy: 10 mg three times daily (30 mg/day), adding 20 mg/day every third day; optional 20–40 mg/day p.r.n. at a time was available for cravings or important inter-current stress or anxiety. Since cravings appeared during afternoons or evenings, dosages were divided unequally: lower in mornings, i.e. on day 31 (230 mg/day) I took 50 mg, then 90 mg, then 90 mg.

Primary outcome measures included, in addition to abstinence from alcohol, the personal assessment of indifference to alcohol (speech, sight, places or odour in restaurants) under any circumstances (stressful situations or anxiety), of cravings, preoccupation and alcohol dreams.

Other outcome measures included the personal assessment of anxiety, muscular tension, quality of sleep, general well-being and side-effects of baclofen. Blood tests assessing haematological parameters, biochemistry, including liver enzymes, were performed at the third and fifth months.

RESULTS

I have not had a drink since January 9, 2004. Detoxification was marked by less malaise than with benzodiazepines. From day 1, anxiety was substantially reduced, muscular tension had begun to subside and sleep had become restful. At the onset of cravings, I took an additional 20–40 mg of baclofen that induced a state of deep relaxation within the hour, followed by somnolence. During the deep relaxation phase it was much easier for me to use CBT and AA techniques to resist drinking. During cravings, the knowledge that I could reliably limit the struggle to 1 h with the additional baclofen dose, was very useful. Since day 15 not one alcohol dream occurred (normally more than once a month). On day 37 (February 14, 2004), on 270 mg/day of baclofen (3.6 mg/kg), I experienced no craving or desire for alcohol for the first time in my alcoholic life. Even in a restaurant with friends, I was indifferent to people drinking. This had never occurred before. Somnolence prevented me from increasing the dosage of baclofen further, and there was no need for the extra 20–40 mg dose. For 12 days, at 270 mg/day, absence of craving persisted, and I remained indifferent to alcohol. In this condition, somnolence became an inconvenient side-effect, and I therefore progressively reduced the dosage to 120 mg/day (1.6 mg/kg) from days 49–63. Since day 63 I have stabilized the dosage around this value with occasional additions of 40 mg p.r.n. in stressful situations. I have not experienced somnolence again; muscular weakness never occurred and there were no other side-effects. Blood tests remained within normal limits.

At the end of my ninth month of complete liberation from symptoms of alcohol dependence, I remain indifferent to alcohol. Abstinence has become natural to me. I no longer plan my life around alcohol. Alcohol thoughts no longer occur. I undertook personal and professional projects, which I was unable to do so before as I had to anticipate consequences of unpredictable drinking episodes (cancelling appointments when possible and blackouts). As taught in CBT, I avoided places, situations, social settings, and vacations where alcohol might have been present. I no longer notice liquor sections in supermarkets. Some of these changes have been pointed out to me by relatives and friends.

I no longer suffer anticipatory anxiety of relapse, of embarrassing or dangerous alcohol-related situations. I am no longer depressed about having an incurable stigmatizing disease.

Liberation from symptoms of alcohol dependence substantially improved my self-esteem.

DISCUSSION

I have never come across a report of complete medication-induced suppression of craving or other symptoms and consequences of alcohol dependence in AA, CBT, rehabilitation centres or in the medical literature.

Here, I describe how, using high-dose baclofen, I succeeded in completely suppressing all signs and consequences of alcohol dependence, while simultaneously and for the first time controlling comorbid refractory anxiety for the ninth consecutive month. However, I wish to underline the 'personal point of view' aspect of this report, since I did not use validated scales to evaluate cravings, anxiety and depression.

Notion of symptom-suppressing dose (SSD)

The baclofen dosage that suppressed my craving and other symptoms of alcohol dependence (SSD) was 270 mg/day (nine times the dosage used in clinical alcohol dependence studies). But the subsequent maintenance dose of ~120 mg/day (1.6 mg/kg) that controlled anxiety prevented craving from reoccurring altogether. This suggests that the maintenance dose is much lower than the SSD. I attained the SSD empirically. In clinical trials, I believe that the SSD (leading to complete indifference to repeated exposure to the strongest cues) should be determined clinically, based on the patient's feedback to the physician and the use of validated scales. I had no choice but to initiate and conduct dose escalation under my sole supervision. But escalation should be tested solely under properly designed studies and should be not replicated by any patient without a strict medical surveillance, which may require an inpatient condition, because of risks associated with somnolence, possible muscular weakness and other side-effects of baclofen.

Issue of well-being, comorbidity and compliance

My alcoholism did not appear in a vacuum: chronic anxiety had long preceded alcoholism. I used alcohol as a tranquilizer until it became an addiction. Associations between alcohol and most substance use disorders and independent mood and anxiety disorders are overwhelmingly positive and significant (Grant *et al.*, 2004). Alleviation of anxiety promotes well-being, which renders 'extra' relief from alcohol useless.

A recent trial established the superiority of topiramate over placebo in improving the quality of life of alcohol-dependent individuals (Johnson *et al.*, 2004). The authors point out that such effects (that were not assessed beyond the 12-week duration of the trial) may be obtained only with moderately dependent alcoholics. The severity of my dependence and anxiety might explain why I did not benefit from topiramate.

A recent multicentre trial showed the advantage of monthly intramuscular naltrexone depot over oral naltrexone in improving the total abstinence rate because of compliance issues with oral naltrexone (Kranzler *et al.*, 2004). Naltrexone—as disulfiram, acamprosate and topiramate—does not claim efficacy in reducing symptoms of anxiety. In contrast, baclofen, by its additional effect on anxiety, encourages compliance and represented an effective monotherapy for me.

Deep relaxation

During cravings, it had always been extremely difficult for me to apply CBT techniques because the efforts required induced anxiety in such a context. In contrast, in the first 37 days during which cravings were present (escalating baclofen doses), when deep relaxation occurred after an additional baclofen dose, it was much easier for me to use CBT and AA techniques to combat cravings and avoid drinking than before. Deep relaxation reliably occurred within the hour after an additional 20–40 mg of baclofen.

Tolerance

Tolerance, though uncommon, has been reported in spasticity after years of intrathecal baclofen therapy, requiring minor adjustments in dosage (Nielsen *et al.*, 2002). Should tolerance develop, there is ample room for me to safely increase the dosage until other medications demonstrate efficacy.

Possible mechanisms of action of baclofen

Medications that facilitate GABA neurotransmission (baclofen, topiramate) show promise in treatment of alcohol and cocaine dependence (Addolorato *et al.*, 2000, 2002a,b; Johnson *et al.*, 2003, 2004; Shoptaw *et al.*, 2003; Kampman *et al.*, 2004). GABA neurotransmission is an important common denominator in the pathophysiology of anxiety and mood disorders (Brambilla *et al.*, 2003; Nemeroff, 2003). GABA modulation is a highly probable mechanism by which the clinical expression of alcohol dependence is blocked by baclofen. However, at high doses, recruitment of additional mechanism(s) by baclofen cannot be excluded. Behaviours that resemble human diagnostic criteria for addiction have been recently described in rats (Deroche-Gamonet *et al.*, 2004). This new animal model should allow further research on the mechanisms by which baclofen reverses dependence.

Chronic treatment

Currently, I use baclofen primarily to control anxiety. It is impossible for me to know whether symptoms of dependence would reoccur, and at which lower dosage, since I have not contemplated weaning myself off baclofen. Would conscious cognition that I have remained indifferent to alcohol for several months modify my behavioural response if symptoms were to reoccur? I believe that the new situation created by baclofen-mediated suppression of symptoms of alcohol dependence offers a window of opportunity to explore the effects of other approaches, such as CBT, in helping reduce or suppress requirement for life-long baclofen treatment. Moreover, the necessity for life-long baclofen treatment could be studied in the newly described addiction model in rats (Deroche-Gamonet *et al.*, 2004).

The major limitation of this report is that it is a self-case report, not a study. But it suggests a new concept of treatment: the blockade of the expression of substance dependence symptoms with simultaneous intervention on anxiety. This case could result from a placebo effect, but I believe this to be unlikely since there has been no report of such complete and prolonged effects in clinical trials. The efficacy of high-dose baclofen should be tested for reproducibility in randomized trials under strict medical surveillance to confirm the validity of the concept of dose-dependent suppression of symptoms of alcohol dependence.

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