Suppressing addiction using high-dose baclofen, rather than perpetuating it using substitution therapy

Olivier Ameisen

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Dear Editor

The perspective by Chick and Nutt (2011) offers a courageous criticism of the barriers to treatment of alcohol and substance dependence, particularly the notions of 'failure of will' and 'moral rather than medical problem'.

Yet, the very idea of 'substitution therapy', that is 'a drug as substitution for a less poisonous drug', which as the authors note has been seen for centuries as the only possible treatment for substance dependence is of serious concern. Why, in contrast to any other affliction in medicine for which treatment is directed towards its pathophysiology, should addiction be the only disease for which treatment should, instead, aim only at mitigating the disease's consequences as if they were an inescapable fate, when an alternative evidence-based model of suppression of addiction already exists (Ameisen, 2005a, 2005b)?

The advent of 'substitution therapy' has revolutionized medicine in the past century and continues to do so mainly in endocrinology. Insulin, cortisol and thyroid hormones are indispensible for survival. Lack of production of these hormones results in death. Replacement/substitution therapy represents a *sine qua non* condition for survival.

None of the drugs of abuse, alcohol, heroin, cocaine or nicotine, are necessary for survival. To the contrary, they are highly toxic and proven to contribute to shortening life expectancy. Their replacement should therefore not been seen as a goal if other avenues exist.

Only decades ago, when their intrinsic mechanisms had not been elucidated, hypertension and heart failure were known to be related to excess sodium chloride (NaCl) consumption. First-line therapy for these conditions was 'abstinence' from NaCl. Often though, patients were simply unable to 'abstain'. This resulted in 'binges' of NaCl that frequently led to deadly pulmonary edema. A moral stigma was attached: these patients were regarded as 'weak-willed' and their deaths as 'self-inflicted'. Later, patients were presented with 'substitution therapy' for NaCl in the form of potassium chloride (KCl). However, most patients found it a 'poor' substitute in terms of taste and many still died from NaCl 'binges'.

The understanding of the renin–angiotensin system led to the advent of angiotensin-converting enzyme inhibitors. These medications address the mechanisms of hypertension and heart failure. Blood pressure is simply normalized by these and other medications that regulate the underlying biological dysfunction. The prognosis of hypertension, recently one of the deadliest diseases, has been transformed. These treatments are not referred to as 'substitution therapy' for sodium and 'abstinence' from NaCl is no longer required. There are numerous other examples: statins are not 'substitution treatment' for cholesterol and fats and strict 'abstinence' from eggs is no longer required from patients with coronary artery disease.

For alcoholism, though, rather than pursuing the thought that the disease can be pathophysiologically suppressed, as my model of cure suggests (Ameisen, 2005a, 2005b), the belief system persists that, as for other addictions (e.g., heroin, cocaine) effort-mediated abstinence aided by 'substitutes', less poisonous agents, represents the sole therapeutic method. One has to keep in mind that methadone, which is used as a substitute for heroin, is a drug of high toxicity. Although it represents less than 5% of opioid prescriptions dispensed in the United States, methadone is implicated in one third of opioid-related deaths (Webster et al., 2011).

In alcohol dependence (AD), clinical evidence (Bottlender and Soyka, 2004), recently corroborated by imaging studies (Heinz et al., 2010), has overwhelmingly shown craving to be the strongest risk factor for relapse. One can infer from this that in alcoholics, any treatment that leaves the patient with any degree of craving will result in relapse. In fact, no such treatment has ever been shown to suppress relapse.

Animal models have proven remarkably dependable translational models for addiction in humans. Of all drugs quoted by the authors as possible 'substitutes' for alcohol, it has to, again, be emphasized that, with the sole exception of baclofen, not a single one *suppresses* motivation, the urge to consume alcohol in animals (Ameisen, 2005a, 2005b).

Benzodiazepines, clomethiazole, tiagabine, vigabatrin, pregabalin, gabapentin, acamprosate, naltrexone, GHB, topiramate, ondansetron and baclofen at low dose (≤1 mg/kg, the dose range used in randomized trials in humans: 30 and 60 mg/day) have all been shown to *at best reduce* motivation to consume alcohol in rats. By contrast, baclofen is the only medication proven to

State University of New York Downstate Medical Center, Brooklyn, NY, USA

Corresponding author:
Olivier Ameisen, Department of Medicine, SUNY Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203, USA
Email: oameisen@hotmail.com

suppress motivation to consume alcohol in rats, but its effect is dose-dependent. Conversely, in human alcoholics, not one of the above-mentioned 'substitutes' has been reported to *suppress* AD in a single individual treated with the medication or with a placebo, except for baclofen, but at doses always higher than the 30 or 60 mg/day used in clinical trials. My self-case report, in which I self-experimented with my model of cure using high-dose baclofen, represents *the first report of medication-induced suppression of AD in the medical literature*. For this reason, I have proposed to change the paradigm '*reduction* of AD with effort-mediated abstinence' to '*suppression* of AD with, as a consequence, effortless indifference to alcohol' (Ameisen, 2005a).

For over a decade, in human alcoholics, Addolorato et al. (2000, 2011) have meticulously and consistently proven that baclofen at 30 or even 60 mg/day can, at best, *reduce but not suppress craving*, forcing patients to deploy efforts to fight the remaining cravings to try to achieve abstinence. Likewise, Caputo et al. (2007) have thoroughly proven that GHB, alone, or even in combination with naltrexone, can, as in animal models, *at best reduce craving* in human alcoholics.

My model of baclofen dose-dependent suppression of AD has been successfully replicated, not only in individual case reports (Bucknam, 2007; Agabio et al. 2007), but high-dose baclofen has been shown to also effortlessly suppress AD in 88% of 60 alcohol-dependent patients. The dose required ranged from 60 to 300 mg/day (Ameisen, 2011). Furthermore, in a series of 300 alcoholics, high-dose baclofen has been shown to effortlessly suppress AD in 91% of the patients (Fred Levin, associate professor of psychiatry, Feinberg School of Medicine of Northwestern University, personal communication).

The fact that medication-induced suppression of AD had never been reported in the medical literature until 2004 and that suppression of alcoholism has since taken place in hundreds of patients in the hands of experienced academic physicians, but solely with the use of one medication, high-dose baclofen, can no longer be brushed aside as some kind of a non-event. It is for the first time that suppression of symptoms and consequences of AD is being consistently reported. Therefore, should not an evidence-based change of paradigm be urgently required in this deadly and devastating disease, especially in light of the fact that substitution treatments throughout decades have never been shown to reduce mortality of alcoholism?

Conflict of interest

The authors declare no conflict of interest in preparing this letter.

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