REGULAR ARTICLE

Baclofen for Binge Eating: An Open-Label Trial

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ABSTRACT

Objective: Baclofen is a GABA-B agonist that may be useful in the treatment of substance use disorders, and also reduces 'binge-like' eating in rodents. We hypothesized that baclofen might be effective in reducing binge eating episodes in binge eating disorder (BED) and bulimia nervosa (BN).

Method: Seven women with BED (n = 4) or BN (n = 3) took baclofen (60 mg/day) for 10 weeks.

Results: Six out of seven patients completed the full 10-week trial. Five out of seven participants (3 BED; 2 BN) demonstrated 50% or greater reduction of frequency of binge eating from beginning to end of the study. Three out of seven participants (2 BED; 1 BN) were free of binge eating at study end. Four out of seven participants elected to continue baclofen at study end. Baclofen was well tolerated by the participants.

Conclusion: In this open-label trial, baclofen was associated with decreased binge eating frequency in patients with BED and BN. © 2007 by Wiley Periodicals, Inc.

Keywords: baclofen; binge eating; bulimia nervosa; eating disorder; addiction; clinical trial

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Introduction

Several lines of evidence suggest an interrelatedness of disorders of binge eating [i.e. bulimia nervosa (BN), binge eating disorder (BED), and anorexia nervosa, binge-purge subtype (AN-BP)] with the substance use disorders. Core diagnostic criteria for substance use disorders and BN/BED suggest symptom overlap between the disorders.[1] Additionally, comorbid substance use disorder rates are particularly high among patients with BN or a binge eating component to their eating disorder.[2–5] While the precise nature of the relationship between substance use disorders and disorders of binge eating remains to be clarified, these lines of evidence suggest that treatments that are effective for substance use disorders may have utility as novel treatments for disorders of binge eating.

Baclofen is a centrally acting γ-amino-butyric acid B [GABA-B] receptor agonist that may be useful in the treatment of substance use disorders. In animal models of repeated drug use, baclofen reduces self-administration of a variety of drug reinforcers, including cocaine,[6] *d*-amphetamine,[7] methamphetamine,[8] ethanol,[9] nicotine,[10] and heroin.[11] Clinical trials of baclofen in the treatment of alcohol, cocaine, and opiate use disorders have yielded encouraging results. In a randomized, double-blind placebo-controlled trial of baclofen in alcohol dependent patients, baclofen was effective in inducing abstinence from alcohol as well as reducing alcohol intake, alcohol craving, and state anxiety.[12] Following initial reports of utility in reduction of craving and use in cocaine dependence,[13,14] a double-blind, placebo-controlled study of baclofen for cocaine dependence revealed decreased cocaine use in patients taking baclofen as reflected in the number of cocaine-free urine toxicology results. Other primary outcome measures, including study retention and cocaine craving, were not affected by baclofen.[15] Similar indications of at least mild treatment effects have been found in methamphetamine dependence,[16] as well as in a double-blind, placebo-controlled trial in maintenance-treatment of opiate dependence,[17] in which treatment retention in the baclofen group was higher but number of drug-free urine samples did not differ. Baclofen, which is used clinically primarily as a muscle relaxant (usual dose range 20–80 mg/day), is generally well-tolerated, with few significant side effects, and no addictive properties.[12,15–18]

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Baclofen appears to affect feeding behavior in some circumstances. A recent review[14] of these data suggests that while baclofen appears to reduce the reinforcing effect of drugs and alcohol in animals, it does not affect responding for other positive reinforcers such as food or water. Other animal studies using baclofen in feeding conditions have varied widely, with some studies showing decreased food intake,[19–21] and others showing increased intake.[22,23] Additionally, previous groups have demonstrated the ability to induce binge-type eating on highly-palatable foods in laboratory animals using both fat-rich and highly sweet meals.[24] Given the possibility that normal vs. pathological feeding may differ mechanistically, baclofen was recently tested in the model of binge-like fat consumption. As compared with a control condition of continuous chow as well as a continuous fat-matched diet, baclofen reduced fat intake in the induced binge-type conditions,[25] suggesting potential utility in binge eating behavior. Baclofen also reduced responding for fat selectively in a similar experiment using an operant responding paradigm to fat vs. normal chow pellets,[26] indicating that baclofen's effects may be specific to fat intake.

Taken together, there is evidence to support the idea that baclofen might be clinically useful in reducing binge eating. Therefore, we conducted a pilot, open-label study of the utility of baclofen in reducing the frequency of binge eating in women with BN and BED.

Method

Participants

Participants were treatment-seeking women between the ages of 18–45, who met DSM-IV criteria for BED or BN. All participants were medically stable, not pregnant or lactating and free of medication, except oral contraceptive pills or over the counter medication. They did not meet criteria for psychotic disorders, bipolar disorders, severe anxiety or depressive disorders, or substance use disorders (mild/moderate depressive and anxiety spectrum disorders were not excluded due to their high comorbidity with BED/BN). The Institutional Review Board of the New York State Psychiatric Institute/Columbia University approved this research protocol, and all participants signed informed consent prior to beginning the study.

Procedure

After an initial phone interview, participants who were eligible and interested in the study came to the clinic for an in-person evaluation, where eligibility was further assessed and consent was obtained. Within 2 weeks of the initial screening visit, patients were assigned a study psychiatrist and began treatment with baclofen. Baclofen was initiated at a dose of 15 mg/day (divided into three doses prior to meals) for 3 days, then raised to 30 mg/day for 3 days, then to 45 mg/day for 3 days, and finally to a maximal dose of 60 mg/day for the remainder of the 10-week study. The dose was lowered if significant side effects occurred.

Patients were asked to maintain a diary recording the number of binge eating and purging (if applicable) episodes and the number of pills taken each day. Diaries were collected at each visit and reviewed by the patient's study psychiatrist. Participants also completed clinical assessments at baseline and at study end, including the Beck Depression Inventory (original version)[27] and the Food Craving Inventory-II,[28] a 28-item scale asking individuals to rate degree of craving for a variety of different food items, from "never" (rating = 1) to "always/almost every day" (rating = 5; total score range = 28–140). Patients were evaluated by their study psychiatrist weekly during the first 3 weeks of the trial, and every other week thereafter, with scheduled phone checks between sessions. Blood was collected for routine clinical testing at the initial screening visit and at week 9 of the trial.

The primary outcome measure was percentage reduction in weekly binge eating episodes between the baseline period of the trial (the medication-free period prior to initiating baclofen treatment, varying from 1 to 2 weeks) and study end (average of weeks 9–10, or last 2 weeks of the trial if not completing the trial).

Results

Seven female participants (4 BED; 3 BN) were recruited for the study. Clinical characteristics of participants are listed in **Table 1**. All participants reached the maximum dose of medication (60 mg/day), and six out of seven patients completed the full 10-week trial. One participant (BED) terminated the study early at week 5 due to lack of medication effect.

Five out of seven participants (3 BED; 2 BN) demonstrated 50% or greater reduction of frequency of binge eating episodes per week from beginning to end of the study (**Table 2**). Three out of seven participants (2 BED; 1 BN) were free of binge eating episodes at study end. Four of the seven participants chose to continue baclofen following trial completion. Except for one subject whose weight increased by 9 lbs without reduction in binge

TABLE 1. Clinical characteristics of pilot participants

Pt no.	Dx	Age	Duration of Illness (years)	Number of Past Medication Trials for ED	Comorbid Psychiatric Diagnoses (Lifetime)	BMI (Baseline)
1	BED	43	36	2	None	31.2
2	BED	35	18	0	MDD; PTSD sxs (past)	29.8
3	BED	40	28	3	OCD; MDD (past)	46.3
4	BED[a]	43	2	3	AN (past)	23.1
5	BN	28	16	3	SocPho; PD (past); PTSD sxs (past)	22.9
6	BN	25	4	2	MDD	24.4
7	BN	28	10	5	AN (past)	19.1

Notes: BED, binge eating disorder; BN, bulimia nervosa; MDD, major depressive disorder; PTSD sxs, posttraumatic stress disorder symptoms (not clearly meeting full criteria for the disorder); OCD, obsessive-compulsive disorder; AN, anorexia nervosa; SocPho, social phobia; PD, panic disorder.
Diagnoses were concurrent unless labeled "past."
[a] Note that one patient (Patient 4) met criteria for BED but was of normal weight.

TABLE 2. Clinical measures over the 10-week trial, by participant

Pt no.	Dx	Weeks of Trial Completed	Weekly Binge Eating Episodes-Baseline	Weekly Binge Eating Episodes-Study End	% Change in Binge Frequency	Change in Weight (lbs.)	Change in BDI	Change in FCI–II
1	BED	10	5	0	−100%	−5	−8	−28
2	BED	10	1[a]	0	−100%	+3	−10	−36
3	BED	5	3	1.5	−50%	0	+6	−15
4	BED	10	9	7	−22%	+9	+2	+5
5	BN	10	12	10	−19%	+1	−8	−18
6	BN	10	4	0	−100%	−1	+3	−16
7	BN	10	9	4	−56%	+2	−2	0
AVG		9	6	3	−64%	+2	−2	−15
p				0.003		0.26	0.34	0.03

Notes: BED, binge eating disorder; BN, bulimia nervosa; BDI, Beck Depression Inventory; FCI-II, Food Craving Inventory II.
[a] One participant reported a higher frequency of binge eating (3–4 times/week) on initial screening procedures, but frequency of binge eating dropped to one episode per week upon beginning baseline study monitoring.

frequency, there was minimal change in weight from beginning to end of the study.

The average decrease in Food Craving Inventory-II scores from baseline to study end was 15. While this was a small change in the Food Craving Inventory-II (14% decrease), it was a statistically significant change (see **Table 2**; $p = 0.03$, two-tailed paired t test). Four of the five patients with greater than 15-point reductions on the Food Craving Inventory-II reported a 50% or more reduction in binge eating. Beck Depression Inventory scores did not change significantly.

Baclofen was well tolerated. The most frequently reported side-effect of baclofen was sedation. Two patients experienced minor adverse events during the trial. One participant experienced mild edema in her legs, likely associated with earlier sunburn. This subject reported not finding the medicine helpful and opted to discontinue the medication (week 5). A second participant had a minor, persistent rash prior to beginning baclofen. Around week 10, her dermatologist recommended she discontinue any nonessential medications. This participant was not considered to have terminated early because she had already completed 10 weeks of the trial at the time she withdrew. Neither adverse event was clearly attributable to baclofen.

Discussion

In this small sample, baclofen reduced the frequency of binge eating episodes by at least 50% in the majority of participants. Baclofen was well tolerated. The fact that four patients wanted to continue the medicine also indicated likely efficacy and tolerability. Baclofen also had a small but statistically significant effect on ratings of food cravings. Given the small number of new agents introduced for treatment of binge eating, these data are of interest. Sufficient clinical response was demonstrated to indicate that a larger, more definitive trial is warranted.

These results are provocative at two levels: they are intriguing beyond the possible utility of the drug for binge eating symptoms. The ability of baclofen to reduce intake, craving and anxiety in animal and human studies of substance abuse provides support for baclofen's effect on abnormally

functioning reward-related neural circuitry.[6] In fact, some of the most intriguing data on the use of baclofen in cocaine abuse come from association of the clinical studies with neuroimaging data. Areas of the brain that have been frequently implicated in drug seeking and craving, including the anterior cingulate cortex and amygdala, are activated selectively in cocaine abusers watching drug-related videos. These areas demonstrate reduced activation when these same cocaine-abusing patients are given oral baclofen at doses lower than those used in this study.[6] Recent studies have also indicated functional abnormalities in the anterior cingulate cortex in patients with BN.[29,30] Given baclofen's demonstrated effect on this circuitry in patients with substance use disorders, the positive effect of baclofen in this trial further suggests the relevance of these brain areas to binge eating symptoms.

Several constructs have been proposed which may help account for the overlap between substance use disorders and eating disorders. Degree of impulsivity[31] and "sensitivity to reward"[32] have been proposed as two symptomatic dimensions upon which the overlap between disorders of binge eating and substance use disorders might be based. These constructs may be interrelated, in a model in which "top-down" (or cortical) inhibition of subcortical regions (e.g. reward-related regions such as the ventral tegmental area-nucleus accumbens dopamine projections implicated in addictions), may be disrupted. In such a model, abnormal functioning of the anterior cingulate cortex could itself lead to impulsivity (via dysregulation of connections to areas such as the orbitofrontal cortex) as well as reward dysregulation (from functional abnormalities in connections to ventral tegmental-nucleus accumbens projections).[33] In fact, the ventral tegmental projection receives GABAergic inputs, with ventral tegmental dopamine neurons containing GABA-B receptors,[34] and stimulation of these receptors decrease the firing of the dopamine projections to the nucleus accumbens. While speculative, baclofen's possible therapeutic role in binge eating as well as substance use disorders may be mediated through decrease of dopamine release in reward-related regions, which may have a stabilizing effect on reward-related circuits.[35]

There are several limitations to this initial trial. The most significant limitation is the small number of participants. Other limitations include the lack of double-blind/placebo-controlled design, the short duration of the baseline measurement period (only 1–2 weeks of self-monitoring of binge eating symptoms prior to initiation of medication), and the known high placebo response rate in BED.[36]

Conclusion

In conclusion, in this pilot open-label trial, baclofen was associated with a reduction in binge eating frequency in patients with BED and BN. These results indicate that a larger, placebo-controlled study of baclofen in the treatment of BED and BN may be warranted. These results also provide further support for translational research between substance use disorders and eating disorders.

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