An Open-Label Study of Citalopram in the Treatment of Pathological Gambling

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Background: This study evaluated the effectiveness of citalopram in the treatment of pathological gambling.

Method: Fifteen adult pathological gamblers (DSM-IV criteria) were administered citalopram in an open-label fashion for up to 12 weeks. Subjects were rated at baseline and at 2-week intervals on measures of gambling severity and depression, and monthly on quality of life.

Results: Patients reported significant ($p < .05$) improvements on all gambling measures including the number of days gambled, the amount of money lost gambling, preoccupation with gambling, and urges to gamble. Thirteen (86.7%) of the patients were rated as "much improved" or "very much improved" on a clinician-rated Clinical Global Impressions scale for gambling. Patients reported improvement in depression and overall quality of life. Patients with major depressive disorder (MDD) (N = 8) improved to approximately the same degree as patients without MDD (N = 7). For most patients, clinical improvement occurred during the first 2 weeks of treatment; for the 9 patients who completed the entire 12-week trial, these gains were maintained.

Conclusion: Citalopram appears to be an effective treatment for pathological gambling, and this benefit was independent of its antidepressant properties. Future studies employing a control group will be important to examine the extent of the response to nonspecific factors of treatment.

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Pathological gambling is increasingly a public health concern because of the greater access to legal forms of gambling. Recent epidemiologic studies estimate that pathological gambling affects 1.2% to 3.4% of the adult U.S. population, with higher prevalence rates in parts of the country where gambling is more accessible.[1,2] Pathological gambling is associated with high rates of psychopathology, particularly substance use disorders,[3–5] depression,[6,7] marital and occupational impairment,[8] and suicidal behavior.[8]

Pathological gambling has variously been conceptualized as an impulse-control disorder, an addictive disorder, and, most recently, as an obsessive-compulsive spectrum disorder. The phenomenological similarities between pathological gambling and obsessive-compulsive disorder (OCD) include difficulties controlling and resisting thoughts and urges to perform repetitive behavior, an increased sense of discomfort or tension before engaging in the behavior or when attempting to resist the behavior, and a sense of gratification or tension relief after performing the behavior.[9,10]

Case reports suggest that pathological gambling may be successfully treated with carbamazepine,[11] lithium,[12] naltrexone,[13,14] and clomipramine.[15] In the only published controlled trials, Hollander and colleagues,[16,17] using single- and double-blind, placebo-controlled crossover designs, demonstrated that the selective serotonin reuptake inhibitor (SSRI) fluvoxamine was effective for the treatment of pathological gambling. However, few subjects in these studies had problems with machine gambling, the principal form of problem gambling in recent studies of pathological gambling. Moreover, the effect of treatment on pathological gambling independent of depression was not examined.

SSRIs are generally considered the treatment of choice for OCD and related conditions.[18] Other impulse-control disorders that have been hypothesized to be obsessive-compulsive spectrum disorders, such as kleptomania, compulsive buying, and trichotillomania, have been shown to be responsive to SSRIs.[19–21] Because pathological gambling and OCD may be related conditions, we conducted an open-label study examining the effectiveness of the SSRI citalopram for the treatment of pathological gambling.

METHOD

Participants were recruited through advertisements in the local newspaper in Providence, R.I. Patients were excluded if they had a clinically significant unstable medical disorder that might affect their ability to participate. Psychiatric exclusion criteria included a current or past history of a psychotic disorder, current mania or hypomania, current drug or alcohol dependence, organic mental disorders, and being judged by the treating psychiatrist to be a significant suicidal risk. Because of the high comorbidity between pathological gambling and other psychiatric disorders and to maintain the generalizability of the study, we did not exclude patients with a current depressive, anxiety, eating, or impulse-control disorder. Patients who were engaged in individual or group psychotherapy were eligible to participate as long as there was no change in the type or frequency of therapy during the course of the study or during the 3 months prior to entering the study.

Twenty patients aged 18 to 70 years with DSM-IV pathological gambling who had gambled at least once per week prior to screening were eligible to participate. The patients were interviewed by R.B.B., who administered the Structured Clinical Interview for DSM-IV (SCID).[22] The evaluation incorporated a pathological gambling diagnostic module modeled on the format of the other modules in the SCID (available from the authors on request). Patients also completed the South Oaks Gambling Screen (SOGS),[23] which has been shown to be a reliable and valid screening test for compulsive gambling, as well as 3 other self-administered questionnaires assessing depression, gambling behavior, and demographic characteristics (the Obsessive Compulsive Drinking Scale modified for pathological gambling [OCDS-PG],[24] the Diagnostic Inventory for Depression [DID; M.Z.; T. Sheeran, Ph.D.; D. Young, Ph.D.; available from the authors on request], and another questionnaire assessing gambling behavior and demographic characteristics [available from the authors on request]). Gambling behavior assessed by questionnaire was reviewed during the diagnostic interview. In a larger reliability study that included each of the patients from the present report, agreement between the questionnaire and interview assessments was high (mean amount of money lost in past month, r = 0.98, N = 25; mean number of days gambled in past month, r = 0.77, N = 25).

Patients were seen every 2 weeks during the 12-week treatment study. At baseline and at each of the 6 follow-up visits, patients were interviewed with the Yale-Brown Obsessive Compulsive Scale modified for pathological gambling (YBOCS-PG).[25] Joint-interview reliability of the YBOCS-PG was determined in 8 patients (r = 0.99 for total score). At each follow-up visit, the interviewer determined the number of days gambled and the amount of money lost since the previous visit and rated the Clinical Global Impressions (CGI) of Improvement[26] in gambling behavior. At each visit, patients completed the OCDS-PG and the DID. The DID is a new self-report depression questionnaire that closely maps onto the DSM-IV diagnostic criteria for depression. In a study of 630 psychiatric outpatients, the DID demonstrated high internal consistency (Cronbach $\alpha = .90$) and test-retest reliability (r = 0.84) (M.Z.; T. Sheeran, Ph.D.; D. Young, Ph.D., submitted for publication). The correlation between the DID and the Beck Depression Inventory was 0.83. The DID was similarly well-correlated with 2 clinician-rated measures of depression, the Hamilton Rating Scale for Depression (0.73) and the Clinical Global Index of Depression Severity (0.73). These correlations are in contrast to a mean correlation coefficient of 0.34 with 19 other measures that evaluate symptoms of other disorders such as OCD, generalized anxiety disorder, and alcohol and substance abuse. Hence, the measure demonstrated good convergent and discriminant validity. The patients completed the Quality of Life Enjoyment and Satisfaction Questionnaire[27] on a monthly basis.

Differences between pretreatment and posttreatment scores were compared using paired t tests. For patients who returned for at least 1 follow-up visit but dropped out prior to completing the study, we used the last-observation-carried-forward method of analysis.

Patients who participated in the 3-month treatment study were prescribed citalopram in an open-label fashion. A flexible dosing schedule was employed. The starting dose for most patients was 10 mg/day, which was subsequently increased to a maximum of 60 mg/day depending on response and side effects.

RESULTS

Five of the 20 patients did not return for a follow-up visit after the baseline evaluation and are not included in our analyses. There were no significant differences in demographic or clinical characteristics between patients who did and did not return for a follow-up visit. The majority of the 15 patients enrolled in the study were male (60.0%, N = 9). Seven patients (46.7%) were married, 5 (33.3%) were separated or divorced, and 3 (20.0%) were never married. All but 1 of the patients were white (93.3%, N = 14), and all but 2 were high school graduates (86.7%, N = 13). The mean ± SD age of the patients was 44.1 ± 10.1 years.

At baseline, all subjects were gambling at least 1 day per week, and 53.3% (N = 8) were gambling at least 3 times per week. The mean amount of gambling debt was $30,564 ± $45,228 (range, $400–$150,000), and a mean of $1890 ± $2512 was lost during the 2 weeks prior to the initial evaluation. The primary forms of problem gambling were machine gambling (N = 12), lottery scratch-off tickets (N = 2), and cards with slot machines (N = 1).

Table 1. Change in Symptom Domains in Pathological Gamblers With and Without Major Depressive Disorder Treated With Citalopram[a]

Group	Baseline Mean (SD)	LOCF Mean (SD)	t (df)	p Value
All patients (N = 15)				
YBOCS-PG score	26.4 (7.6)	5.4 (4.9)	8.85 (13)	< .005
OCDS-PG score	31.6 (6.5)	6.4 (4.9)	10.16 (14)	< .005
$ Lost in 2 wk	1877 (2520)	145 (324)	2.58 (14)	.02
Days gambled in 2 wk	8.8 (5.2)	1.6 (1.7)	5.63 (14)	< .005
DID score	29 (12.1)	6.4 (10.8)	8.95 (14)	<.005
With major depressive disorder (N = 8)				
YBOCS-PG score	29.4 (5.6)	5.3 (5.0)	11.80 (6)	< .005
OCDS-PG score	30.0 (7.3)	6.3 (5.2)	5.99 (7)	< .005
$ Lost in 2 wk	2331 (3231)	49 (103)	2.34 (7)	.05
Days gambled in 2 wk	8.1 (5.4)	1.1 (1.4)	3.82 (7)	< .01
DID score	32.9 (9.1)	10.0 (14)	7.40 (7)	< .005
Without major depressive disorder (N = 7)				
YBOCS-PG score	23.4 (8.4)	4.7 (5.2)	4.32 (6)	< .01
OCDS-PG score	33.4 (5.4)	6.6 (5.0)	8.97 (6)	< .005
$ Lost in 2 wk	900 (743)	254 (455)	1.84 (6)	.12
Days gambled in 2 wk	9.6 (5.3)	2.1 (2.0)	3.88 (6)	< .01
DID score	24.6 (14.2)	2.3 (2.8)	5.10 (6)	< .005

[a]Abbreviations: DID = Diagnostic Inventory for Depression, LOCF = last observation carried forward, OCDS-PG = Obsessive Compulsive Drinking Scale Modified for Pathological Gambling, YBOCS-PG = Yale-Brown Obsessive Compulsive Scale Modified for Pathological Gambling.

Figure 1. Amount of Money Lost During 3-Month Course of Treatment With Citalopram

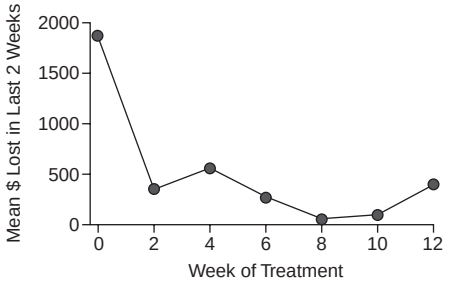
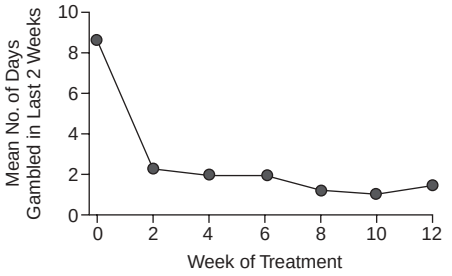


Figure 2. Number of Days Gambled During 3-Month Course of Treatment With Citalopram



The mean duration of problem gambling was 6.9 ± 9.2 years (range, 0–33 years), and the mean age at onset was 37.2 ± 12.1 years (range, 21–56 years). The mean SOGS score was 14.6 ± 2.6. The mean score on the YBOCS-PG was 26.4 ± 7.6, and on the OCDS-PG, 31.6 ± 6.5. Approximately half (53.3%, N = 8) of the patients were diagnosed with major depressive disorder (MDD) at baseline. The mean DID score (29.0 ± 12.1) indicates a mild-to-moderate level of severity of depression in the sample. The most common current nondepressive comorbid disorder was panic disorder (20.0%, N = 3).

Nine of the 15 patients who returned for at least 1 follow-up visit completed the 3 months of the study. The 6 patients who dropped out did so after 2 (N = 1), 4 (N = 1), 6 (N = 3), and 8 (N = 1) weeks of treatment. One patient dropped out due to side effects, and 1 dropped out due to lack of efficacy; the remaining 4 patients dropped out for unknown reasons.

The mean daily dose of citalopram at the time of the final evaluation was 34.7 ± 14.6 mg.

The data in Table 1 show that the patients significantly improved on all outcome measures during the course of the study. Scores on the YBOCS-PG decreased by 79.5%, and the OCDS-PG scores dropped by 79.7%. The mean amount of money lost during a 2-week interval, compared with baseline, dropped by 92.3%, and the mean number of days gambled decreased from nearly 9 days to less than 2 days during a 2-week period. Thirteen patients (86.7%) were rated on the CGI as much or very much improved, and during the 2 weeks prior to the last follow-up visit, 5 patients (33.3%) did not gamble at all. Patients reported that their overall quality of life had improved. Whereas 10 patients (67%) rated their quality of life at baseline as "poor" or "very poor," 11 patients (73%) rated their quality of life at the last observation as "good" or "very good."

Patients' level of depression also significantly improved (see Table 1). In all patients, the correlation between the change on the YBOCS-PG and the DID from baseline to the last visit was 0.19 (p > .10, NS). To determine whether improvement in gambling was due to the antidepressant properties of citalopram, we compared improvement in gambling behavior in patients who were and were not diagnosed with MDD. Significant reductions in gambling were found in both groups, and the degree of improvement was comparable (see Table 1).

Finally, we examined the time course of improvement. Figures 1 through 5 show that most of the improvement on all measures occurred by the time of the first follow-up visit. Of the 13 patients who were ultimately rated "much improved" or "very much improved" on the CGI, 7 (54%) experienced that improvement at the time of the first follow-up visit.

Figure 3. Yale-Brown Obsessive Compulsive Scale Modified for Pathological Gambling (YBOCS-PG) Scores During 3-Month Course of Treatment With Citalopram

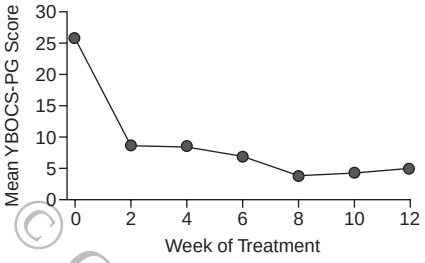


Figure 4. Diagnostic Inventory for Depression (DID) Scores During 3-Month Course of Treatment With Citalopram

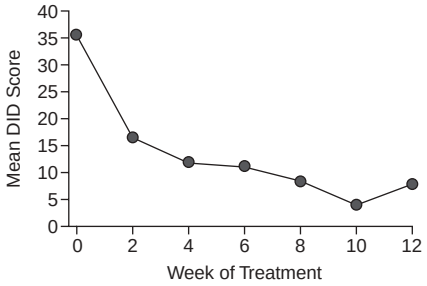
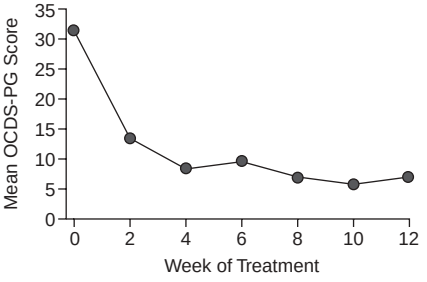


Figure 5. Obsessive Compulsive Drinking Scale Modified for Pathological Gambling (OCDS-PG) Scores During 3-Month Course of Treatment With Citalopram



DISCUSSION

The results of this study suggest that citalopram may be an effective medication for the treatment of pathological gambling. Some patients stopped gambling entirely, and others reduced their gambling behavior and lost much less money than they had been losing before the study began. Half of the patients had concurrent MDD; however, reduction in gambling was found to be comparable in gamblers with and without MDD. Thus, improvement in gambling could not be attributed solely to improvement in depression. In addition to symptom reduction, patients also reported an improvement in the quality of their lives.

Half of the patients who ultimately improved had done so by the time of their first follow-up visit. This early response might represent placebo response or improvement related to nonspecific factors associated with treatment. It is noteworthy, though, that 5 of the 6 patients who were rated much or very much improved on the CGI at the time of the first follow-up visit maintained their improvement throughout the duration of the 12-week trial (1 of the 7 patients who improved at the first follow-up dropped out after this visit). This is suggestive of a true medication response rather than a placebo response, which is characterized by rapid response followed by deterioration over time.[17,28]

Nonetheless, placebo response is important to consider in interpreting the results of studies of obsessive-compulsive spectrum/impulse-control disorders. For example, Black and colleagues[20] reported that fluvoxamine was effective in an open trial of the treatment of compulsive buying, whereas Ninan et al.[29] failed to find a significant benefit of fluvoxamine in a double-blind placebo-controlled study. Similarly, Koran et al.[21] found that fluoxetine significantly reduced hair-pulling behavior in an open-label study of trichotillomania, whereas 2 double-blind crossover studies did not find a significant difference between fluoxetine and placebo.[30,31]

The 2 recently published treatment studies of pathological gambling by Hollander and colleagues[16,17] demonstrated a marked and rapid placebo response. In the first study,[16] 10 patients were treated with placebo for 8 weeks followed by 8 weeks of active medication. After 2 weeks of placebo treatment, total scores (urges plus behavior) on the YBOCS-PG decreased by 51.8%. In their second study[17] of 10 pathological gamblers, there was a 44% reduction in YBOCS-PG scores during the 1-week single-blind placebo lead-in. In the present study, the mean percentage drop in YBOCS-PG scores from baseline to visit 1 was 66.4%, and this increased to 76.5% at endpoint. The continued and maintained improvement of the patients in the present study contrasts with Hollander and colleagues'[16] finding that the amount of improvement on the YBOCS-PG declined slightly from 51.8% at 2 weeks to 47.4% at the end of 8 weeks of placebo treatment.

A comparison of the patients treated in the present study and by Hollander et al. raises several other issues that may be important to consider in future pharmacotherapy treatment studies of pathological gambling. Patients with comorbid mood or anxiety disorders were included in ours as well as Hollander and colleagues' studies. We found that gamblers with and without MDD responded equally well to citalopram.

The gamblers in our study in Rhode Island and Hollander and colleagues' studies in New York were comparable in the severity of pathological gambling as reflected by their scores on the SOGS and YBOCS-PG; however,

there were marked differences in the principal form of gambling activity. In the 2 New York studies, half of the patients identified betting on horses or sports as their principal gambling activity, whereas only 3 of the 20 patients were machine gamblers. Moreover, the mean duration of problem gambling was approximately 20 years. In contrast, in our Rhode Island sample, the primary problem was machine gambling in almost all patients (13/15). Although the mean age of our patients was 2 and 5 years older than the mean ages of the patients in the 2 New York samples, the mean duration of problem gambling was 13 years less. In fact, the duration of problem gambling was 5 years or less in two thirds of the Rhode Island gamblers, whereas the minimum duration of problem gambling in the New York samples was 6 years. It therefore seems that the gamblers studied by us in Rhode Island and by Hollander and colleagues in New York, while representative of their respective geographical regions, may be clinically different. Future studies of pharmacotherapy with pathological gambling will need to consider the impact of patient characteristics such as type of gambling problem and duration of problem gambling on treatment response.

Drug names: carbamazepine (Tegretol and others), citalopram (Celexa), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), naltrexone (ReVia).

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