An Open-Label, Flexible-Dose Study of Olanzapine in the Treatment of Trichotillomania

Rege S. Stewart, M.D., and Vicki A. Nejtek, Ph.D.

Background: Thus far, only selective serotonin reuptake inhibitors have been systematically studied in the treatment of trichotillomania, and the results are conflicting. This open-label study is the first to systematically evaluate an atypical neuroleptic, olanzapine, as a monotherapy in the treatment of trichotillomania.

Method: Twenty-one patients were screened and 18 patients were enrolled in a 3-month open-label study of olanzapine for trichotillomania (diagnosis based on modified DSM-IV criteria). Patients with comorbid psychiatric disorders or on treatment with psychoactive medication were excluded. Olanzapine was titrated gradually in 2.5-mg/week increments up to a maximum dose of 10 mg/day.

Results: Seventeen patients who completed at least 1 week of olanzapine treatment were evaluated. Hair pulling, as measured by the Massachusetts General Hospital Hairpulling Scale, decreased by 66% from baseline ($p \leq .001$), and mean scores on the Hamilton Rating Scale for Anxiety decreased by 63% ($p \leq .05$). Clinical Global Impressions scale scores also revealed significant improvement as a whole ($p \leq .001$), with 4 patients having complete symptom remission at the end of the study period.

Conclusion: Findings suggest that olanzapine may be an effective monotherapy for trichotillomania.

(J Clin Psychiatry 2003;64:49–52)

Received Sept. 17, 2001; accepted May 3, 2002. From the Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, Dallas.

Supported by a grant from Eli Lilly and Company, Indianapolis, Ind.

These data were presented as a poster at the 154th annual meeting of the American Psychiatric Association, May 9, 2001, New Orleans, La., and at the 41st annual meeting of the New Clinical Drug Evaluation Unit, May 20, 2001, Phoenix, Ariz.

Dr. Stewart has received grant/research support from Eli Lilly and Company, Merck, Parke-Davis, SmithKline Beecham, Zeneca, Glaxo, Solvay, Hoffman-LaRoche, Pfizer, Upjohn, Wyeth-Ayerst, Ciba-Geigy, and Besselaar; has been on a speakers/advisory board for Forest, Pfizer, SmithKline Beecham, and Wyeth-Ayerst; and is a major stock shareholder in Abbott. Dr. Nejtek has been on a speakers/advisory board for AstraZeneca.

The authors thank Joseph T. Gilbert, R.N., and Humera A. Chowdhary, M.D., for their clinical research assistance, and Jane A. Coleman, A.A., for clerical contributions.

Corresponding author and reprints: Rege S. Stewart, M.D., The University of Texas Southwestern Medical Center at Dallas, 5959 Harry Hines Blvd., POBI, 6th floor, Dallas, TX 75390-9101 (e-mail: Rege.Stewart@UTSouthwestern.edu.).

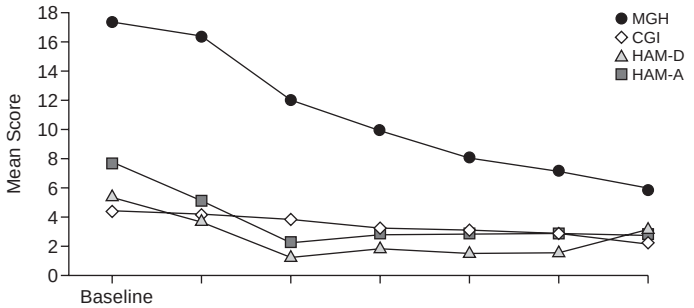
Although trichotillomania is classified in DSM-IV as an impulse disorder, it is often conceptualized as part of the obsessive-compulsive spectrum of disorders due to its ritualistic nature.[1] These observations led to pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs), although controlled and open-label data supporting their effectiveness in trichotillomania are mixed.[2,3] Failure of some patients to respond to an SSRI led to several augmentation strategies including lithium, anxiolytics, and neuroleptics.[4] Marked improvement of trichotillomania was noted by several researchers with the addition of a neuroleptic to an SSRI. These open-label augmentation studies used low-dose pimozide,[5] risperidone,[6] haloperidol,[7] and olanzapine.[8] The results of these studies suggest that neuroleptics may be effective in treating trichotillomania. Since the treatment success reported in prior studies depended on augmentation, the authors of the present study proposed to test the effectiveness of olanzapine monotherapy in treating trichotillomania. Olanzapine is an atypical neuroleptic with more potent blocking of 5-HT_2 than D_2 receptors, and thus less severe extrapyramidal side effects than traditional neuroleptics.

METHOD

Twenty-one patients with trichotillomania were screened after responding to advertisements in a local urban newspaper and a trichotillomania support group newsletter and signing an institutional review board–approved consent form. Eighteen patients met study criteria, but 1 patient dropped out during the first week; thus, 17 patients received at least 1 week of medication. Daily uncontrollable hair pulling resulting in noticeable hair loss was an inclusion criterion. The operational definition of trichotillomania in this study was broader than as defined by DSM-IV, since many of our patients did not feel gratification or a sense of relief as a result of their hair pulling, but all reported increased tension prior to their ritual. Patients with current comorbid psychiatric diagnoses or recent use of psychoactive medications were excluded. One treatment-refractory patient who had been receiving 200 mg/day of sertraline for over 2 years was allowed to participate.

Our sample (N = 17) consisted of 2 African American and 15 white women with a mean ± SD age at trichotillomania onset of 15.1 ± 11.5 years and duration of illness of

Figure 1. Treatment With Increasing Olanzapine Doses Results in Significant Reduction in Hair Pulling and Improvement in Mood Scores at Weeks 4, 6, 8, and 12[a]



	Week 0	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12
Mean dose, mg/d	0	0	2.5	4.4	6.0	8.0	8.5
Mean score							
MGH	17.2	16.2	11.9	9.9**	8.0**	7.1***	5.8***
CGI	4.4	4.1	3.8	3.3**	3.1***	2.7***	2.2***
HAM-D	5.4	3.7	1.3	1.9**	1.5**	1.6**	3.1
HAM-A	7.6	5.0	2.2	2.8**	2.7**	2.8**	2.8*

[a]Abbreviations: CGI = Clinical Global Impressions scale, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, MGH = Massachusetts General Hospital Hairpulling Scale.
*p ≤ .05.
**p ≤ .01.
***p ≤ .001.

20.5 ± 10.4 years. Using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID),[9] we determined that none of the patients had met criteria for another Axis I diagnosis in the last 6 months. Six patients had been treated in the past for major depressive disorder, and an additional 3 had minor depressive symptoms. Two of our patients were treated in the past for obsessive-compulsive disorder with complete recovery, and 2 had met DSM-IV criteria for compulsive personality disorder. Four patients had never had any psychiatric symptoms other than trichotillomania. None of the patients had a substance abuse history. Nine patients reported no response to previous SSRI therapy.

At baseline, all patients were assessed using the SCID as well as the Massachusetts General Hospital Hairpulling Scale (MGH),[10] Hamilton Rating Scale for Anxiety (HAM-A),[11] Hamilton Rating Scale for Depression (HAM-D),[12] and Simpson-Angus Scale.[13] In addition, a brief medical examination with selected laboratory tests was administered. Patients were given a hair-pulling diary with instructions to report (1) every instance of hair pulling, (2) the duration of each episode, (3) their ability to resist the urge, and (4) the level of anxiety experienced during the episode. The diary and the MGH hair-pulling scores together formed the basis for determining the overall Clinical Global Impressions scale (CGI)[14] score.

Patients were seen for a review of their hair-pulling diary and were evaluated with the MGH, HAM-A, HAM-D, Simpson-Angus, and CGI at every visit. During the first week, patients were required to fill out a daily hair-pulling diary, but were not treated with medication. Patients began an upward titration schedule of olanzapine starting at 2.5 mg h.s. after week 1 assessments were completed, followed by 5 mg h.s. for week 2 if well tolerated. Afterward, patients were seen every 2 weeks as the titration of olanzapine continued up to the maximum dose of 10 mg h.s. at week 8. The last dose increase occurred at the week-8 appointment, and patients were next seen at the final week-12 visit. The mean dose of olanzapine at each visit is indicated in Figure 1.

Assessment scores from baseline to midway through the study (week 6) and at endpoint (week 12) were analyzed for changes over time using a last-observation-carried-forward (LOCF) technique with a nonparametric Wilcoxon rank sum paired test due to the small sample size. It was determined in advance that patients' scores would be assessed halfway through the study at week 6, since the titration schedule at week 6 would allow us to examine dose efficacy (i.e., 5–7 mg/day) in relation to symptomatology changes. To identify significant relationships among hair pulling, anxiety, depression, and global improvement, a Spearman correlation matrix was performed. A 95% confidence interval and an a priori alpha probability of .05 was set for all analyses.

RESULTS

One patient was lost to follow-up after 1 week of placebo treatment; therefore, 17 patients (mean age = 36.8 ± 12.5 years) completed at least 1 week of olanzapine therapy and were included in the LOCF analysis. Four patients dropped out of the study prior to the week 12 evaluation. Two patients dropped out because of sedation (after 5 and 8 weeks of olanzapine treatment), 1 dropped out because of parotid swelling at week 8, and 1 was lost to follow-up after 1 week of taking 2.5 mg/day of olanzapine. The most common adverse side effects were sedation and weight gain. All of these side effects, including the parotid swelling, resolved on medication discontinuation. No patients developed extrapyramidal symptoms as assessed by weekly administration of the Simpson-Angus.

Significant differences in MGH, HAM-A, HAM-D, and CGI scores between baseline and weeks 4, 6, 8, and 12 are indicated in Figure 1. Changes in scores from baseline to endpoint, determined using the LOCF technique, indicated that hair pulling decreased by 66%, levels of anxiety were reduced by 63%, and depressive symptoms were attenuated by 43%. An improvement of 50% in global impression was recorded.

Statistically significant improvement in MGH, HAM-A, HAM-D, and CGI scores occurred at 6 weeks, when about one half of patients were taking 5 mg of olanzapine and the other half were taking 7.5 mg. At the end of the study, only 6 patients reached a daily dose of 10 mg; the rest were taking 7.5 mg of olanzapine. Our data suggest that the minimum effective dose of olanzapine was 5 mg; 7 patients responded well at 7.5 mg. The MGH score was the primary efficacy variable. We arrived at a CGI score by considering patients' daily hair-pulling diary and MGH score, which is a reliable and validated assessment tool for assessment of trichotillomania.[10]

Although patients reported some anxiety and depressive symptoms at baseline, their level of symptomatology did not meet DSM-IV criteria for an anxiety or depressive disorder. Nevertheless, as patients' hair-pulling rituals decreased, so did their levels of anxiety and depression: mean HAM-A scores decreased from 7.6 to 2.8 and mean HAM-D scores decreased from 5.4 to 1.6 by week 8, as indicated in Figure 1.

A Spearman correlation matrix showed significant relationships among psychiatric assessment and hair-pulling scores. A robust association between MGH and HAM-A and HAM-D scores emerged by week 12, so that a decrease in hair pulling was significantly related to a decrease in anxiety ($p = .02$) and depressive symptoms ($p = .005$). At every observation timepoint, including baseline, HAM-A and HAM-D scores were significantly related, with correlation coefficients ranging from 0.75 to 0.54. Except at baseline, MGH and CGI scores were also highly associated, with coefficients ranging from 0.76 to 0.63. There was a significant reduction in depressive symptoms of 72% at week 6 ($p \leq .01$), but minimal reduction by week 12 due to 2 patients becoming more depressed at weeks 10 and 11 of the study.

Four of the 13 patients who completed the 12-week study stopped their hair pulling completely and reported no urge to pull their hair during the previous 4 weeks. At baseline, each of these patients pulled their hair daily on multiple occasions. Three of our patients had large bald spots; 2 of these patients wore wigs. All 3 patients were free of bald spots at the end of the study. On the other hand, 1 patient who pulled only her eyelashes did not improve at all. The rest of the patients improved from multiple daily hair pulling to once or twice per week. We have data on 1-month follow-up after olanzapine discontinuation on 12 patients. Four patients relapsed and 8 maintained their improvement, although only 1 was totally free of urges to pull.

DISCUSSION

While all of the patients reported increased anxiety and tension preceding their hair pulling, some were not even aware of the behavior until well into their ritual. Chronicity of behavior may have accounted for these findings, since the mean duration of illness in our sample was 20.5 ± 10.4 years. Another possibility to consider is that patients who ritualistically pull their hair without conscious awareness may suffer from a tic spectrum disorder. The robust response to olanzapine, a dopaminergic agent, would support such a consideration.

It is noteworthy that 2 of our patients developed major depressive disorder at the end of the study while on treatment with 10 mg of olanzapine, elevating the mean HAM-D score to near the week 1 level. One of these patients had a past history of recurrent major depressive disorder, but the other had no previous depression. This finding was unexpected, especially since Shelton et al.[15] reported that olanzapine augmentation was reported to significantly improve depressive symptoms in patients who were unresponsive to fluoxetine treatment alone. In view of our findings, trichotillomania patients should be carefully monitored for possible emergence of depressive symptoms when olanzapine is used as a monotherapy for trichotillomania. Since comorbidity with depression and anxiety is high among trichotillomania patients, a combination of SSRI and olanzapine treatment may be more appropriate for trichotillomania patients who are depressed.[16]

Our study suggests that olanzapine may be effective in reducing core hair-pulling symptoms, as well as associated anxious and depressive symptoms of trichotillomania. The major limitation of this study is that it is not a double-blind randomized protocol; therefore, some investigator bias may have been inadvertently introduced. It should also be noted that the hair-pulling diary may be considered a form of behavioral therapy, which may confound our findings. The fact that as the olanzapine dose was gradually increased, the MGH score steadily decreased argues against that hypothesis. In addition, there was no statistically significant difference in MGH score between baseline and the end of week 1, even though patients did keep a hair-pulling diary but were not taking medication.

Drug names: fluoxetine (Prozac and others), haloperidol (Haldol and others), olanzapine (Zyprexa), pimozide (Orap), risperidone (Risperdal), sertraline (Zoloft).

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