Clinical Study

Sustain Released Bupropion in the Treatment of Trichotillomania: Outpatient Follow Up Survey

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Objectives. Trichotillomania (TTM) is more common than expected. SSRI’s are the treatment of choice in TTM. However, response rates are lower with SSRI’s. The aim of our study is to explore other pharmacological interventions.

Materials and Methods. Nine female TTM patients with SSRI treatment failure were included. Sample was treated with bupropion SR up to 450 mg/day.

Results. Six out of nine patients responded well to bupropion SR. Massachusetts General Hospital Hair Pulling Scale (MGH) demonstrated a significant improvement at the twelve week point ($t: 32.3$, power: 1, lambda: 97.1, $P < .0001$) and the response rates remained stable at sixteen-month follow up visit.

Conclusions. Bupropion SR could be an alternative pharmacological treatment for TTM. Larger samples with double blind placebo controlled design are needed to confirm our preliminary report.

1. Introduction

Trichotillomania (TTM) is primarily a female dominated disorder [1], classified in the DSM-IV as an impulse control disorder with the essential feature being recurrent and maladaptive impulsive skin picking behavior. In the International Classification of Diseases of the World Health Organization, TTM is coded under the heading of Habit and Impulse Disorders together with kleptomania, pyromania and pathological gambling [2]. Impulse control disorders are characterized by an overwhelming urge to perform a harmful act. TTM is a chronic, progressive, disorder, which has a prevalence of 0.8% to 1.4% among US adults [1, 3, 4].

TTM is classified as an impulse control disorder since the early 90’s, and is believed to be related to Obsessive Compulsive Spectrum Disorders [5–7]. A genetic link between the disorders had been identified, with increased rate of OCD among relatives with TTM [8]. OCD is currently classified as an anxiety disorder, and is characterized by recurrent intrusive thoughts (obsessions) and/or repetitive mental or behavioral rituals performed in response to obsessions or according to rigid rules (compulsions). OCD and TTM share overlapping co-morbidity, familial transmission and possible treatment response. Both are characterized by difficulties suppressing inappropriate repetitive behaviors, suggesting underlying dysregulation in inhibitory control processes [9]. Case series, double blind studies demonstrated the effectiveness of the SSRI treatment in TTM [10–13]. Short-term treatment with SSRI’s was effective in most cases, however in the long term follow up three major problems occurred [1]. Studies with larger samples could not demonstrate the same effective results [2]. The drop-out rates were high, and compliance rates were relatively low in order to measure intermediate and long term outcome [3]. Most of the patients became non responders to the SSRI treatment even when the dose of the treatment drug was increased to the upper limits [14].

Clinicians preferred to switch to another SSRI but the same “desensitization procedure to SSRI treatment” was repeated [15, 16]. The mixed clinical results caused questions about the possible classification of TTM [8, 9, 17]. OCD spectrum theory was not strong enough to explain the treatment response. Genetic studies [18–20], classification studies [9, 17] and pharmacological treatment studies [11–14, 21–23] brought the possibility of addictive behavior in trichotillomania.

2. Materials and Methods

Nine TTM female patients received up to 450 mg/d Sustained Release Bupropion (SR) due to trichotillomaniac behavior, up
to a twelve month period. After twelve months of treatment full responders decreased and stopped the medication in four weeks. This patient group completed another three-month follow up without medication. Trichotillomanic behavior was measured with The Massachusetts General Hospital Hair Pulling Scale (MGH). The patients also completed the Hamilton Rating Scale for Depression-17 items (HRSD) [24] and Hamilton Rating Scale for Anxiety (HRSA) [25].

The mean age of the patients was 24.1 ± 6.8 and the duration of illness was 5.4 ± 3.9 years. All the patients were diagnosed as TTM at least two years before the participation in the survey. Eight out of nine were treated with various SSRIs regimes such as Fluoxetine up to 60 mg/d \((n = 1)\), paroxetine up to 80 mg/d \((n = 2)\), citalopram up to 80 mg/d and sertraline and fluvoxamine up to 200 mg/d (one patient for each drug). One patient received clomipramine up to 225 mg/d.

Five patients were responders but relapsed after tapering of the medication (clomipramine, paroxetine, sertraline), and four were partial responders (fluoxetine, fluvoxamine, paroxetine, citalopram). The partial and nonresponders received another trial of SSRI with escitalopram up to 40 mg/d without significant success before the bupropion SR trial.

All the patients completed full medical work up that included physical examination, ECG, blood pressure, laboratory work up (CBC, chemistry that includes liver enzymes, thyroid functions, FSH, LH, estrogen levels) and urine screening. All patients were in good health condition, except three with mild to moderate obesity \((BMI \approx 34.6)\). None of the patients reported use of addictive substances and/or alcohol. All the patients suffered primarily from TTM and not from other Axis I diagnosis. However, three patients reported mild anxiety and depression symptoms during the psychiatric interviews.

Patients started with 150 mg/d bupropion sustained release (SR) and in one week reached to 300 mg/d. After two weeks of 300 mg/d treatment, the dosage increased to 450 mg/d. All the patients were stabilized with 450 mg/d treatment for another nine weeks.

3. Results

All participants tolerated well the bupropion SR treatment. Three of them complained about side effects such as nausea, headaches, dry mouth, and nervousness. None of the patients stopped the medication due to the side effects.

At twelve weeks of treatment six out of nine patients were considered to be responders and one patient was partial responder. In The Massachusetts General Hair Pulling Scale the average score was 17.1 ± 2.02 in the recruitment phase of the study. At week eight the score dropped to 8.67 ± 6.1 and at week twelve the score decreased to 7.55 ± 5.9. ANOVA test with repeated measures demonstrated a significant decrease in the hair pulling behavior of TTM patients \((f: 32.3; \text{power}: 1, \lambda: 97.1, P < .0001)\). The HSRA also demonstrated a modest improvement of the anxiety symptoms. HRSA scores were 19.2 ± 1.4 at the beginning. At week twelve the score dropped to 15.7 ± 2.7. ANOVA test with repeated measures found the improvement to be significant \((f: 7.9; \text{power}: 0.99, \lambda: 23.6, P < .0008)\).

The HSRA did not show any significant improvement in TTM group. HRSD (21 item) scores were at 12.7 ± 2.4 baseline. At week twelve the scores dropped to 11.7 ± 2 which was found to be statistically significant in ANOVA test with repeated measures \((f: 2.43; \text{power:} 0.58, \lambda: 7.3, P < .09)\).

Nonresponders were not included in the follow up phase of the survey and received higher dosage of bupropion SR with benzodiazepine combination. Five out of seven responders completed the follow up period. Two dropped out due to missing visits. All remained subjects were fully responded to treatment for twelve months period and bupropion SR gradually decreased in three weeks period. These patients were followed up for another three months. Only one patient reported relapse at three-month follow up period. The response to the treatment remained statistically stable in the follow up period \((7.9 ± 5.9)\) in MGH scale. This was found to be a nonsignificant statistical result versus the twelve week results of the study \((t\text{-test}, P < .09)\)

4. Discussion

This is one of the first surveys to look at the use of bupropion in the treatment of TTM, in patients nonresponders to SSRI pharmacotherapy. The results of our study suggest that bupropion SR is well tolerated and may be beneficial in reducing picking behavior. We note that the improvement seen in the study subjects does not appear to be related to an antidepressant effect of bupropion, since the HRSD scores, except for three patients, were within normal limits at baseline and did not change significantly at the 12-week endpoint.

The pharmacological approach to TTM represents a field receiving growing interest in recent years. To date, a range of pharmacological agents have been reported to be useful for the treatment of trichotillomanic behavior and related urges with the most convincing evidence coming from studies with SSRIs [11–14, 21], followed by the mood stabilizers [23] and the opioid antagonist naltrexone [22]. A standard pharmacological approach for TTM, however, is far from being established, and in the case of SSRIs, a double blind study failed to show partial efficacy of SSRI treatment [14]. It has been proposed that TTM is a heterogeneous disorder which overlaps with both OC spectrum disorders [6–8] and addictive disorders [22, 23], and some authors have hypothesized that there are specific subtypes of trichotillomania with specific patterns of treatment response within this population [8].

However, Lochner et al. notes significant differences between OCD and TTM. In contrast to compulsions in OCD, hair pulling in TTM is not a response to obsessive thoughts, but rather due to an irresistible urge and the promise of gratification. In addition, whereas OCD symptoms change over time in terms of focus and severity, TTM patients usually only present with hair pulling without evolution [8].
Addictive parameters of TTM are behavioral pathology characterized by obsessive-compulsive seeking, and consequently obtaining, the substance of choice (in this case—hair pulling, skin picking, and gambling), with progressive loss of control of behavior [26]. Our group had also previously reported of similarities between TTM and pathological gambling (PG).

There are two major neurological pathways involved in addiction. First, the mesolimbic dopamine reward pathway, which is essential for survival, can be physically altered by drug abuse to result in uncontrolled cravings. Second, the decision-making prefrontal cortex, which suppresses inappropriate reward response, can also be altered by drug abuse. Further, addicts can be predisposed to addiction by genetic defects in reward pathway neurotransmission and stress-related developmental brain abnormalities. Relapse to addictive behavior can occur because of stress or cue-related reward pathway stimulation or even by a single drug dose or behavior [27]. Bupropion acts at the mesolimbic pathway level, and is also structurally related to amphetamine and the sympathomimetic diethylpro- pion [28–30]. The known comorbidity between TTM and attention deficit/hyperactivity disorder [28] as well as the association between TTM and impulsive behavior [31] have led investigators to postulate that bupropion may represent a logical treatment option in TTM [30].

We propose that bupropion may represent a pharmacological option for SSRI nonresponders since bupropion does not appear to work via serotonergic pathways [28, 31, 32]. Several preliminary studies suggest that bupropion SR may have a role in the treatment of PG [33, 34]. Bupropion SR selectively inhibits the reuptake of DA and NA, which in turn stimulate acetylcholine, hydroxytryptamine, and GABA receptors as well as endorphins [30]. All of these psychoactive systems may play a role in the pattern of urges, cravings, and sense of enjoyment seen in pathological gambling behavior and disorders of chemical addiction. Bupropion has been shown to reduce nicotine withdrawal symptoms and the urge to smoke, and has FDA approval for the treatment of nicotine dependence [29, 32]. In a small single blind trial, bupropion was also shown to be helpful in the treatment of comorbid cocaine abuse and ADHD [29]. Two case reports have described the successful use of bupropion in amphetamine addiction [28], and in both cases, amphetamine withdrawal symptoms and amphetamine cravings were significantly reduced. Whereas naltrexone has already been investigated for the treatment of urges and cravings associated with TTM [22], bupropion SR, which has more affordable side effect profile, may represent a useful alternative for TTM.

The primary limitations in this survey are the open label design and the small sample size. In addition, our results may be influenced by selection bias, since our patients were selected from an ambulatory setting, and patients with comorbid substance dependence and personality disorders were not included in the survey. Since these diagnoses are commonly comorbid with TTM, the results of our study may not be generalizable to patients seen in actual clinical practice. Despite these limitations, however, our outcome survey suggests that bupropion SR may be an effective treatment for TTM. Our results are strengthened by the fact that our patient sample was selected from a group of patients who were considered to be nonresponders to two SSRI trials. Further studies in a larger, more varied patient sample are clearly warranted in order to evaluate the effectiveness of bupropion SR in TTM and, by extension, in other impulsive-addictive spectrum disorders.

References


