Systematic Review: Pharmacological and Behavioral Treatment for Trichotillomania

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Trichotillomania is a psychiatric condition characterized by compulsive hair pulling. Three interventions have been studied in the treatment of trichotillomania: habit-reversal therapy (HRT) and pharmacotherapy with either selective-serotonin reuptake inhibitors (SSRI) or clomipramine. This systematic review compared the efficacy of these interventions in blinded, randomized clinical trials. The electronic databases of Medline, Premedline, PsychINFO, Embase, and the Cochrane Central Register of Controlled Trials were searched for relevant trials using the search terms "trichotillomania" or "hair pulling." Trials were eligible for inclusion if they compared habit-reversal therapy, SSRI pharmacotherapy, or clomipramine pharmacotherapy to each other or placebo and employed randomization and blinded assessment of outcome. Our primary outcome measure was mean change in trichotillomania severity. The summary statistic was standardized mean difference. Seven studies were eligible for inclusion in this review. Overall, meta-analysis demonstrated that habit-reversal therapy (effect size [ES] = −1.14, 95% confidence interval [CI] = −1.89, −.38) was superior to pharmacotherapy with clomipramine (ES = −.68, 95% CI = −1.28, −.07) or SSRI (ES = .02, 95% CI = −.32, .35). Clomipramine was more efficacious than placebo, while there was no evidence to demonstrate that SSRI are more efficacious than placebo in the treatment of trichotillomania. Future studies on trichotillomania should seek to determine if HRT can demonstrate efficacy against more rigorous control conditions that account for non-specific effects of therapy and determine if HRT can be an effective intervention for trichotillomania beyond the few sites where it is currently practiced in research studies. Future therapy and pharmacotherapy studies in trichotillomania should employ larger sample sizes and intention-to-treat analysis and seek to validate clinical rating scales of trichotillomania severity.

Key Words: Clomipramine, habit-reversal therapy, meta-analysis, selective serotonin reuptake inhibitors, systematic review, trichotillomania

Trichotillomania (TTM) is a psychiatric condition characterized by compulsive hair pulling. Despite often being quite impairing and affecting approximately .6% to 1% of the population (1,2), trichotillomania has been rather sparsely studied. The three main therapeutic modalities for trichotillomania that have been studied are: 1) pharmacotherapy with a selective serotonin reuptake inhibitor (SSRI); 2) pharmacotherapy with clomipramine, a tricyclic antidepressant; and 3) habit-reversal therapy (HRT). Recent data from the Trichotillomania Impact Project suggest that pharmacotherapy with SSRI is the most frequently employed intervention to treat TTM (3). A recent review on this topic also recommended that the use of SSRI "such as citalopram ... may be preferable (in relation to clomipramine) given the superior safety and tolerability of this drug class for related conditions, such as obsessive-compulsive disorder (OCD), and the positive results reported for an open-label study with trichotillomania patients" (4). The purpose of this systematic review is to evaluate the evidence supporting the efficacy of these three interventions compared with placebo and to compare the efficacy of these treatment modalities with each other.

Criteria for Considering Studies for This Review

Types of Studies

This review included randomized, controlled, clinical trials published in scientific literature with blinded assessment of clinical outcome.

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Types of Participants

Participants were required to be older than age 16 and have a primary psychiatric diagnosis of trichotillomania or chronic hair pulling by DSM-IV criteria (5).

Types of Interventions

The three interventions included in this study were use of a selective serotonin reuptake inhibitor, clomipramine, or habit-reversal therapy.

Habit-reversal therapy is a cognitive behavioral therapy technique for trichotillomania and Tourette's syndrome (6). The habit-reversal therapy program for trichotillomania consists of four main components.

Self-monitoring. The self-monitoring component has the patient keep records of hair-pulling behavior.

Awareness Training. Awareness training increases patient awareness of both hair-pulling behavior and high-risk situations that frequently trigger hair-pulling behaviors.

Stimulus Control. Stimulus control includes techniques either to decrease opportunities to pull hair or to interfere with or prevent pulling (i.e., wearing gloves in high-risk situations).

Stimulus-Response Intervention or Competing Response Intervention. Stimulus-response intervention is defined as developing activities to substitute when the desire for hair pulling occurs, such as deep muscle relaxation or taking a walk. Competing response intervention is defined as teaching the subject to engage in a physically incompatible behavior (to the pulling) for a fixed period of time (i.e., 1 minute) or until the urge goes away. In HRT, patients are permitted to pull hair only after these activities are completed.

For inclusion in this review, HRT arms of studies were required to include all four of these components. Additional components and techniques could be added to the therapeutic intervention and still qualify for consideration as an HRT intervention for this review.

Acceptable control interventions for pharmacological interventions in this review were either placebo or an active control condition. Active control was defined as any treatment modality

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believed to be ineffective for trichotillomania at the initiation of the study and placed in the design of the experimental protocol as a control condition for the active treatment intervention. Acceptable control conditions for a therapy trial could be wait-list, psychosupportive or psychoanalytic sessions, and any other therapeutic techniques previously studied and deemed minimally or ineffective in the treatment of trichotillomania.

Types of Outcome Measures

Primary Outcomes

Our primary outcome was defined as mean improvement in a clinical scale measuring trichotillomania severity (continuous outcome) conducted by a blinded rater. Acceptable clinical scales for rating of trichotillomania (in their order of preference) included the National Institute of Mental Health Trichotillomania Severity Scale or Trichotillomania Impairment Scale (7), any other measurement of the severity of hair pulling (i.e., counts of hairs pulled out or videotaped ratings of hair loss), or the Clinical Global Impressions Improvement Scale (8). Self-report measures such as the Massachusetts General Hospital Hairpulling Scale (MGH-HS) were only eligible to be the primary outcome measure in double-blind studies—studies in which subjects were blinded to their own treatment assignment (9). In double-blind studies, MGH-HS was the most preferred scale to measure trichotillomania outcome based on its common use and validation in trichotillomania (10).

Search Strategy for Identification of Studies

The electronic databases of PubMed, PsychINFO (1967–2005), Embase (1974–2000), and the Cochrane Central Register of Controlled Trials (CENTRAL, as of 2006, Issue 1) were searched for relevant trials. PubMed was searched using the medical subject headings "trichotillomania" or "hair pulling." PsychINFO, Embase, and CENTRAL were searched with the key words "trichotillomania" or "hair pulling." The references of appropriate papers for this study, as well as any appropriate review articles in this area, were additionally searched for citations of further relevant published and unpublished research.

Methods of the Review

Selection of Studies

The titles and abstracts of studies obtained by the search strategy outlined above were scrutinized by two reviewers (M.H.B. and A.L.-W.) to determine if they were potentially eligible for inclusion in this review.

Eligibility for selection into the study was based on scrutiny of the full articles for the following inclusion criteria: 1) randomized clinical trials with a control group or a comparison between active treatments; 2) blinded assessment of clinical outcome; 3) patient population with a primary psychiatric diagnosis of trichotillomania or chronic hair pulling; and 4) comparison of SSRI, clomipramine, and habit-reversal therapy to each other or a control condition.

Data Collection

Specifically designed forms/coding sheets were used by two reviewers (M.H.B. and A.L.-W.) independently working to collect data on methods, participants, dropouts, interventions, and outcome measurements. Any disagreement between reviewers was resolved through discussion and obtaining more information from the study investigators.

Choice of Summary Statistics

For our primary outcome, mean improvement in trichotillomania severity was measured as standardized mean difference and was pooled for overall meta-analysis. Standardized mean difference was favored over weighted mean difference as the primary outcome because rating scales differed between included studies.

For the inclusion of crossover trials along with traditional parallel-group trials in our cumulative meta-analysis, three different methods were used. These methods were derived from the standard, accepted methodology for incorporating crossover into meta-analysis in the scientific literature (11,12). If there were significant carryover effects observed in the statistical analysis of a crossover study, then data were analyzed only up until the point of the first crossover; thus, only data from the initial, first randomized treatment would be used. If no significant carryover effects were observed and individual subject data were available for baseline and outcome data after each crossover period, then all the data were available to compute the actual measurements of treatment effect needed for this study–mean difference and standard deviation. If individual subject data were not available from the original manuscript, then the reported subject number, mean difference in treatments, and *p* value or *t*-statistic was used to retrieve the standard deviation of paired observations. The mean difference and standard deviation of this measure can be estimated from available data based on two equations:

$$d = Xa - Xp$$

where d equals the difference in means between the active treatment (Xa) and control (Xp); and

$$SD(d) = (d * \sqrt{n})/T$$

where SD(d) is the standard deviation in mean differences between treatments, *n* is the sample size, and T is the *t*-statistic from the paired *t* test of the outcome (11).

The standardized mean difference (effect size [ES] = d/SD[d]) and standard error of standardized mean difference {[*t*(95% confidence interval for n-1 degrees of freedom)/1.96]/$\sqrt{n}$} were computed from the two values above for inclusion in meta-analysis. Crossover and parallel group studies were then incorporated into a single meta-analysis using the generic inverse variation method of RevMan 4.2.8 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). A random effects model was chosen for meta-analysis, as there was considerable heterogeneity between studies.

Assessment of Publication Bias

Relevant data from all the included trials was entered into a funnel plot (trial effect size plotted against sample size) to detect any publication bias (13).

Assessment of Heterogeneity

Heterogeneity of treatment response was assessed from the forest plot of weighted mean differences and relative risk of individual studies. Statistical estimates of heterogeneity were performed using the I-square heterogeneity statistic in RevMan.

Sensitivity Analysis

Sensitivity analyses were conducted to determine the robustness of reviewers' conclusions to methodological assumptions made in conducting this systematic review. In particular, sensitivity analyses were conducted to determine the effects of subject dropout. Our primary outcome measure reported treatment