**Monoamine oxidase inhibitors (MAOIs) for Trichotillomania:**

**A case series**

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**Abstract**

Purpose/Background: Despite several decades of research, there are no US Food and Drug (FDA) approved medications for trichotillomania, nor are medications generally approved in other geographical jurisdictions. Monoamine oxidase inhibitors (MAOIs) show efficacy in the treatment of depression and some possible promise for obsessive compulsive disorder.

Methods/Procedures: We present new data from a case series collected in a specialty clinical practice over a four-year period.

Findings/Results: In five treatment-resistant patients whose trichotillomania had not improved with at least one course of Cognitive Behavior Therapy (CBT) and trials of n-acetyl cysteine (NAC), an antipsychotic and a serotonin selective reuptake inhibitor (SSRI), two had marked clinical improvement (>40% improvement) on phenelzine, one improved on tranylcypromine, and two showed no improvement (<10%) on phenelzine. In two of the three patients who experienced improvement, there was co-occurring depression.

Implications/Conclusions: MAOIs in trichotillomania may deserve large-scale randomized controlled trials, particularly in specialist settings where first-line interventions have proven inadequate to manage severe symptoms.

**Introduction**

Trichotillomania, a disorder characterized by hair pulling that usually results in alopecia (hair loss) and decreased self-esteem, appears to affect approximately 2% of adults (1). Trichotillomania is associated with distress, reduced quality of life, and may even result in serious medical consequences (e.g. repetitive strain injuries or gastrointestinal obstruction due to consumption of hair) (2-4). Yet despite the fairly common nature of the disorder, as well as the negative consequences associated with it, we have yet to determine a first-line pharmacological option for treating trichotillomania. A variety of medications have shown some promise for trichotillomania (including clomipramine, olanzapine and N-acetyl cysteine) (5), but the evidence base is limited.

The use of monoamine oxidase inhibitors (MAOIs) for patients with major depressive disorder, social anxiety disorder, and panic disorder is well established (6-7). Less well recognized by mental health practitioners is that MAOIs have also been found to be potentially promising for other psychiatric disorders, such as PTSD and possibly obsessive-compulsive disorder (8-9). MAOIs are less frequently used by clinicians as compared to many other classes of medication due to drug-drug interactions, the need for patients to comply with a tyramine restricted diet, and the need for an appropriate washout period when switching between certain medications (10). In terms of previous reports, we could find only one use of an MAOI for trichotillomania. Krishnan and colleagues reported the use of isocarboxazid (30mg/d) (isocarboxazid is FDA approved as a second line treatment for major depressive disorder) in a 32-year old man with trichotillomania and comorbid depression (11). He was treated for 4 weeks and both his depression and hair pulling improved. After stopping the medication due to a surgical procedure (requiring discontinuation of this medication), his trichotillomania symptoms returned, and then again improved when the medication was restarted.

The aim of the current study was to examine the treatment response and tolerance of the irreversible MAOIs phenelzine and tranylcypromine in adults with trichotillomania. This was a chart review of all patients with trichotillomania started on an MAOI within the last four years to examine who responded and at what dose and for how long. We hypothesized that MAOIs would potentially be associated with marked symptomatic improvement in a few of these patients.

**Materials and Methods**

Records from consecutive adult outpatients with Diagnostic and Statistical Manual Version 5 (DSM-5) defined trichotillomania as their primary diagnosis who had sought treatment voluntarily in a specialty clinic were evaluated to assess outcomes. All patients had attended the Addictive, Compulsive, Impulsive Disorders specialty clinic at the University of Chicago. All patients who had received phenelzine or tranylcypromine, as monotherapy or in combination with other medications, from 2018 to 2022 were included in the chart review.

The specialty clinic sees, on average, four to six patients each week with trichotillomania. Most patients are offered both behavioral therapy and medications (usually starting with a trial of NAC and then progressing to another glutamate agent, clomipramine or possibly an antipsychotic as monotherapies or augmentations depending upon severity and comorbidities). Using this general approach, it is estimated that approximately 50-60% of patients will report at least some moderate reduction in their hairpulling symptoms. When these approaches do not produce any or limited benefits, however, additional options and the evidence base for their use is more restrictive.

Baseline information included current age, comorbid diagnoses, and trichotillomania symptom severity assessment using the *NIMH Trichotillomania Symptom Severity* scale (NIMH-TSS) (12) as part of routine clinical practice. Total NIMH-TSS scores constituted the *a priori* primary outcome measure. For clinical purposes of examining symptom severity and change over time, patients were rated at each visit using the NIMH-TSS.

In general, patients were started on phenelzine 15 mg twice daily and after one week the dose was increased to 30mg twice daily and then to 45mg twice daily one week later, if tolerated. If started on tranylcypromine, the dose began at 10mg daily and each week was increased by 10mg per day to a target dose of 40mg daily. Patients were told about both options and four of the five chose phenelzine due to perceived benefits while one chose tranylcypromine due to possible weight gain that could occur from phenelzine.

The institutional review board of the University of Chicago approved the chart review. As part of routine clinical care, patients were informed of the off-label use of MAOIs for trichotillomania, the potential for dietary and drug-drug interactions, and were started on a tyramine restricted diet prior to starting the medication. All patients provided informed written consent for treatment and for their anonymized data to be used. The authors assert that all procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

**Results**

 Five patients with trichotillomania were identified who received treatment using an MAOI. An overview of the salient clinical features and changes in symptom severities is provided in Table 1. Chart review indicated that all five patients’ trichotillomania symptoms had not previously improved with at least one course of cognitive behavior therapy (CBT) and trials of n-acetyl cysteine (NAC), an antipsychotic and a serotonin reuptake inhibitor (SRI).

 Three of the five trichotillomania patients experienced clinically significant improvement in their trichotillomania symptoms in response to taking a MAOI (defined as >40% improvement on the NIMH-TSS) (13). Side effects were as expected for this class of medication (Table 1). In cases where the patients improved, they continued on the medication despite side effects.

**Discussion**

 Trichotillomania is a common but often overlooked obsessive-compulsive related disorder, which has few evidence-based treatment options available (5). MAOIs have proven to be a useful treatment option in the context of certain other mental health conditions, particularly when symptoms have proven resistant to usual interventions (6-8). There are also some positive findings in OCD: one randomized trial compared a MAOI to clomipramine and found similar OCD symptom improvements with both treatments (9).

 In this case series, we report that MAOIs were associated with symptomatic improvement (>40% improvement) in 3/5 of the identified patients, all of whom had received multiple prior evidence-based treatments for trichotillomania. While caution is needed in view of the small number of cases, it is possible those with comorbidities were more likely to respond than those without comorbidities (Table 1). This may suggest future clinical trials using MAOIs should permit inclusion of patients with comorbidities (where clinically safe/appropriate to do so), which would also have the benefit of making such samples more representative of the condition at large. The findings highlight the potential value of conducting a large scale appropriately controlled clinical trial using MAOIs in treatment-resistant cases of trichotillomania, and perhaps other obsessive-compulsive related disorders. Based on assumed placebo response rate of 30% for this disorder, and the response to MAOIs observed here of 60%, a sample power calculation suggested that a future study would need a sample size of ~42 per group to detect a significant difference with 80% power, using categorical treatment response on the NIMH-TSS scale. Of course this entails many assumptions. The case series also indicates that MAOIs merit consideration as a treatment option in specialist treatment centers, in cases of trichotillomania that are severe and non-responsive to other treatments. Of course, such treatments require careful consideration of benefits and risks.

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