Published in final edited form as:

Int Clin Psychopharmacol. 2014 September ; 29(5): 266–273. doi:10.1097/YIC.0000000000000036.

Venlafaxine Extended-Release Treatment of Hoarding Disorder

Sanjaya Saxena, M.D. and Jennifer Sumner, Ph.D.

Department of Psychiatry, UCSD School of Medicine

Abstract

Objectives—Hoarding Disorder, classified as a separate disorder in DSM-5, is a common, chronic, and potentially disabling syndrome that can be difficult to treat. Only one prior study prospectively measured response to pharmacotherapy in compulsive hoarders, finding that hoarders responded as well to paroxetine as did non-hoarding OCD patients. However, paroxetine was not tolerated well in that study, and overall response was moderate. Therefore, we conducted an open-label trial of venlafaxine extended-release for Hoarding Disorder.

Methods—24 patients meeting DSM-5 criteria for Hoarding Disorder were treated with venlafaxine extended-release for 12 weeks. All patients were free of psychotropic medications for at least 6 weeks prior to the study. No other psychotropic medications, cognitive-behavioral therapy, organizers, or cleaning crews were permitted during the study. To measure hoarding severity, the Saving Inventory-Revised (SI-R) and the UCLA Hoarding Severity Scale (UHSS) were administered before and after treatment.

Results—23 of the 24 patients completed treatment. Hoarding symptoms improved significantly, with a mean 36% decrease in UHSS scores and a mean 32% decrease in SI-R scores. Sixteen of the 23 completers (70%) were classified as responders to venlafaxine extended-release.

Conclusions—These results suggest that venlafaxine extended-release may be effective for treatment of Hoarding Disorder.

Keywords

Hoarding; Disorder; Venlafaxine; Extended-Release; Treatment; Compulsive; Pharmacotherapy

Introduction

Hoarding is defined as the acquisition of, and inability to discard items even though they appear (to others) to have no value (Frost and Gross 1993). Frost and Hartl (1996) developed the first systematic definition and diagnostic criteria for clinically significant compulsive hoarding: 1) the acquisition of, and failure to discard a large number of possessions that appear (to others) to be useless or of limited value, 2) living or work spaces are sufficiently cluttered so as to preclude activities for which those spaces were designed,

Address correspondence to: Sanjaya Saxena, M.D., Director, UCSD Obsessive-Compulsive Disorders Program, Director, UCSD Outpatient Psychiatric Services, Professor, UCSD Department of Psychiatry, 140 Arbor Drive, San Diego, CA 92103, Telephone: (619) 534-6883, FAX: (619) 543-7537, ssaxena@ucsd.edu.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

and, 3) significant distress or impairment in functioning is caused by the hoarding behavior or clutter. Hoarding and saving symptoms are part of a discrete clinical syndrome that includes the core symptoms of difficulty discarding, urges to save, excessive acquisition, and clutter, as well as indecisiveness (Samuels et al. 2008), perfectionism, procrastination, disorganization, and avoidance (Frost and Hartl 1996). In addition, many compulsive hoarders are quite slow in completing tasks, are frequently late for appointments, and display circumstantial, over-inclusive language. Patients with prominent hoarding and saving who display these other associated features are thus considered to have the “compulsive hoarding syndrome” (Saxena et al. 2002, Steketee and Frost 2003). The bulk of evidence indicates that hoarding is a separate clinical syndrome, quite distinct from obsessive-compulsive disorder (OCD) (Saxena 2007, Pertusa et al. 2010). Therefore, formal diagnostic criteria were developed for “Hoarding Disorder” (Mataix-Cols et al. 2010) and are now included in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (Arlington, VA, *American Psychiatric Association*, 2013). These diagnostic criteria have been found in a clinical field trial to have excellent sensitivity, specificity, inter-rater reliability, and validity (Mataix-Cols et al. 2013).

Compulsive hoarding is driven by an exaggerated perceived need to keep and save items, often related to obsessional fears of losing items that the patient believes are valuable or may be needed later, or making the “wrong” decision about what to keep or discard (Saxena et al. 2002, Steketee and Frost 2003). These fears cause substantial distress and lead to compulsions to save items. Hoarders also frequently have excessive emotional attachments to possessions and distorted beliefs about the importance of possessions (Frost and Gross 1993). Excessive acquisition behavior, including acquisition of free items, excessive buying, and stealing, are quite common, found in 65–85% of all compulsive hoarders (Mueller et al. 2009, Frost et al. 2009, Timpano et al. 2011). The consequent clutter often causes significant social and occupational impairment (Frost et al. 2000, Saxena et al. 2002, Tolin et al. 2008a, Saxena et al. 2011) and adverse effects on the family members of compulsive hoarders (Tolin et al. 2008b). In severe cases, it can produce health risks from infestations, falls, fires, and inability to cook or eat in the home (Steketee and Frost 2003). Avoidance is prominent and includes behavioral avoidance of discarding or storing items, and cleaning, as well as cognitive avoidance of making decisions or even thinking about the clutter.

In community-based population samples, clinically significant compulsive hoarding is common, with a population prevalence of 1.5–5.8% (Samuels et al. 2008, Mueller et al. 2009, Iorvelino et al. 2009, Timpano et al. 2011; Nordsletten et al. 2013). Initial onset of compulsive hoarding symptoms is usually around 12–13 years of age (Frost and Gross 1993, Samuels et al. 2002, Grisham et al. 2006, Ayers et al. 2010, Tolin et al. 2010a). The course tends to be chronic and progressive, with severe levels of hoarding starting in the mid-thirties, and symptoms often worsening with age (Grisham et al. 2006, Ayers et al. 2010, Tolin et al. 2010a).

Some retrospective studies investigating the influence of OCD symptom factors on treatment response found that hoarding and saving symptoms in patients with OCD were associated with poor response to pharmacotherapy with serotonin reuptake inhibitor (SRI) medications (Black et al. 1998, Winsberg et al. 1999, Mataix-Cols et al. 1999, Stein et al.

2007 & 2008, Salomoni et al. 2009), but many others have failed to replicate this association (Saxena 2011). Several studies found that hoarding/saving symptoms had no significant effect on response to treatment in OCD patients (Alonso et al. 2001, Ferrao et al. 2006, Erzegovesi et al. 2001, Shetti et al. 2005, Landeros-Weisenberger et al. 2010). In addition, a family study that compared a large group of hoarding OCD patients with non-hoarding OCD patients found that a very similar proportion of patients in the two groups reported moderate response or total remission with SRI treatment, as well as for behavioral therapy (Samuels et al 2007). Thus, hoarding is clearly not a consistent predictor of poor response to SRI medications.

Unfortunately, all prior studies except for those by our group examined only patients who met diagnostic criteria for OCD, and most used diagnostic or screening instruments, such as the Structured Clinical Interview for DSM-IV (SCID - First et al. 1995), that exclude patients who have compulsive hoarding but no other OCD symptoms (who comprise > 80% of all Hoarding Disorder patients), so they may not be generalizable to the broader population of compulsive hoarders (Saxena 2007). Moreover, none of the retrospective studies monitored, focused on, or measured hoarding symptoms apart from non-hoarding OCD symptoms, so they could not determine whether hoarding symptoms improved or responded as well as non-hoarding OCD symptoms.

Only one study to date (Saxena et al. 2007) prospectively and quantitatively measured response to standardized pharmacotherapy in patients with the compulsive hoarding syndrome, regardless of whether they had other OCD symptoms. Patients with the compulsive hoarding syndrome (n=32) and non-hoarding OCD patients (n=47) were treated openly with the SRI, paroxetine, for 12 weeks (mean dose 41.6 +/- 12.8 mg/day), according to a standardized protocol. No other medications or cognitive-behavioral therapy (CBT) were allowed during the treatment period. Compulsive hoarders responded equally as well to paroxetine as non-hoarding OCD patients, with significant and nearly identical improvements in OCD symptoms, depression, anxiety, and overall functioning (Saxena et al. 2007). A similar proportion of hoarders and non-hoarding OCD patients were full responders (28% vs. 32%) and partial responders (22% vs. 15%). Hoarding/saving symptoms improved as much as non-hoarding OCD symptoms. The proportion of dropouts was also similar. Compulsive hoarders who completed treatment showed a mean 31% decline in symptom severity. No correlation was found between hoarding severity and treatment response. Both the overall mean reduction of Y-BOCS score (-6.1 points) and the overall categorical response rate of 49% (39 out of 79 patients were classified as responders) were very similar to those reported in the Cochrane review of SRI trials for OCD (Soomro et al. 2008). These results suggested that SRI medications were just as effective for compulsive hoarders as for non-hoarding OCD patients (Saxena et al. 2007).

However, paroxetine was not well tolerated in that study. Only 16 of the 79 patients in the study were able to tolerate the target dose of paroxetine, 60 mg/day. Fewer than half of the sample achieved a dose of 40 mg/day, and 12 patients could not tolerate more than 30 mg/day. The most common side effects limiting dose increases were sedation, fatigue, constipation, headaches, and sexual side effects (Saxena et al. 2007). Compulsive hoarders in both clinical and research settings tend to be middle-aged and older adults, predominantly

women (Steketee and Frost 2003, Tolin et al. 2008, Steketee et al. 2009, Pertusa et al. 2010), and the anticholinergic side effects of paroxetine can be more problematic for such populations. Therefore, we sought to test a medication better tolerated in older populations, which would allow higher doses, known to be more effective for treatment of OCD (Bloch et al. 2010). In addition, the paroxetine study began before specific rating scales for measuring hoarding severity were available, so most subjects in that study could not have their hoarding/saving symptoms measured separately from non-hoarding OCD symptoms. Hence, we sought to assess and quantify the specific response of hoarding symptoms to pharmacotherapy, using more recently developed hoarding symptom rating scales.

We conducted an open-label trial of venlafaxine extended-release for Hoarding Disorder. We chose venlafaxine extended-release primarily for its superior tolerability in middle-aged and older patients, as well as its potential efficacy in patients who have not responded well to more selective SRI's. Venlafaxine has been tested extensively in older populations and has found to be safe and well tolerated (Ibor et al. 2008, Mazeh et al. 2007, Staab and Evans 2000). Venlafaxine appears to be as effective as paroxetine or clomipramine for OCD (Albert et al. 2002, Denys et al. 2003) and is less likely to cause these side effects than those medications. Moreover, venlafaxine may be efficacious for SSRI-refractory OCD (Hollander et al. 2003, Marazziti 2003). We hypothesized that patients with Hoarding Disorder would tolerate venlafaxine extended-release well and show significant symptom improvement in both the core symptoms and associated features of compulsive hoarding, as well as comorbid depression, anxiety, and OCD symptoms.

Methods

This study was approved by the UCSD Institutional Review Board, in accordance with the Declaration of Helsinki. All subjects enrolled gave written informed consent to participate after procedures and possible side effects were explained to them.

Subjects

Subjects were recruited from the San Diego area with flyers, print and internet advertisements, as well as referrals from local clinicians. 24 patients with Hoarding Disorder (21 female, 3 male; mean age = 51.8 +/- 8.1 yrs.; age range 33–61) were enrolled. Nineteen subjects were Caucasian, three were Hispanic, and two were Asian-American. To be enrolled, subjects had to meet DSM-5 diagnostic criteria for Hoarding Disorder as their primary, most distressing or impairing condition. All subjects were diagnosed by clinical interview, followed by administration of the MINI International Neuropsychiatric Interview (MINI - Sheehan et al. 1998). For additional identification of comorbid OCD and related "OC Spectrum Disorders," all subjects were also administered the OCD Spectrum module from a revision of the Structured Clinical Interview for DSM-IV (First et al. 1995) developed by Lochner and colleagues (Lochner et al. 2005). Patients with primary psychotic disorders, bipolar disorder, panic disorder, post-traumatic stress disorder (PTSD), substance abuse/dependence, eating disorders, dementia, or mental retardation were excluded. All subjects were free of psychotropic medication and any other medication that could affect brain function for at least six weeks prior to starting venlafaxine extended-release.

To measure the severity of the component symptoms of hoarding disorder, every subject was administered both the UCLA Hoarding Severity Scale (UHSS - Saxena et al. 2007) and the Saving Inventory-Revised (SI-R - Frost et al. 2004), immediately before and after the twelve week treatment period. The UHSS is a ten-item, clinician-administered scale that assesses the presence and severity of various components of the compulsive hoarding syndrome, including extent of clutter, urges to save items, excessive acquisition, difficulty discarding, social and occupational impairment, slowing, perfectionism, indecisiveness, and procrastination. Scores reflect the average occurrence of each symptom over the one week prior to and including the time of the interview. Its maximum score is 40. The UHSS is a semi-structured interview that allows additional questions for clarification, which helps improve accuracy when assessing patients who may be prone to confusion regarding the meaning of specific questions. Scores are based on the patient's report but may also include information obtained from family members or others, and the final rating depends on the clinical judgment of the interviewer, which is especially important when assessing patients with poor insight. Use of a clinician-administered rating scale is especially important in assessing patients with hoarding disorder, because many compulsive hoarders have poor insight into their condition and symptoms (Steketee & Frost 2003; Pertusa et al. 2010; Neziroglu et al. 2012) and tend to under-report their specific hoarding symptoms, while over-reporting their overall global impression of hoarding severity (Dimauro et al, 2013).

The UHSS is internally consistent and demonstrates convergent, discriminant, and known groups validity (Saxena et al. 2013). It shows good internal reliability (Ayers et al. 2013b) and is strongly correlated with the SI-R across both hoarding and healthy control samples (Saxena et al. 2013; Ayers et al. 2013b). Principle component factor analysis of the UHSS reveals three factors, representing a) associated features and functional impairment, b) clutter and social impairment, and c) excessive acquisition, distress with discarding, and need to save possessions, that account for 58% of the variance (Saxena et al. 2013). The UHSS has been found to differentiate compulsive hoarders from healthy controls with no psychiatric disorders, as well as from patients with OCD who have other symptom domains as their predominant problems, even if they also have some hoarding/saving symptoms (Saxena et al. 2007). The UHSS has also been shown to detect clinically significant changes in hoarding symptom severity with treatment (Saxena et al. 2007; Ayer et al. 2013a). In addition, the UHSS has been found to be a slightly stronger predictor of disability in geriatric Hoarding Disorder patients than the SI-R, uniquely correlating with both extent of limitation and frequency of disability (Ayer et al. 2013b).

The SI-R is a well-validated, 23-item self-report questionnaire with three factor analytically defined subscales for difficulty discarding, excessive clutter, and compulsive acquisition (Frost et al. 2004). It shows good internal consistency and test-retest reliability, as well as known groups validity and concurrent and divergent validity in clinical and non-clinical samples. The SI-R has been found to distinguish hoarders from non-hoarding populations. Its maximum score is 92, and a score of at least 36 has been used as a cutoff for inclusion in studies of compulsive hoarders (Grisham et al. 2006). In order to be enrolled, subjects had to score > 40 on the SI-R and >17 on the UHSS. The SI-R cutoff was based on the results of prior studies that constructed receiver operating characteristic (ROC) curves to distinguish

patients with Hoarding Disorder from controls and other diagnostic groups with maximal sensitivity and specificity (Tolin et al. 2010, Frost and Hristova 2011).

Subjects were also assessed immediately before and after treatment with the Hamilton Depression Rating Scale (HDRS – Hamilton 1960), Hamilton Anxiety Scale (Ham-A – Hamilton 1959), Global Assessment Scale (GAS – Endicott et al. 1976), and Clinical Global Impression/Improvement (CGI) scale. Despite the fact that it is not adequate for assessing the severity or extent of hoarding symptoms, the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS – Goodman et al. 1989) was also administered to assess changes in both hoarding and non-hoarding symptoms, to allow for comparison with older studies that grouped hoarding and non-hoarding symptoms together. “Response” was defined as >30% decrease in UHSS and SI-R scores, and at least “much improved” on the CGI-Improvement scale. These response criteria were based on those found to be optimally predictive of clinical response in OCD (Tolin et al. 2005).

Treatment

All subjects were treated with venlafaxine extended-release for twelve weeks, according to a standardized protocol, but with some flexibility in dosing, based on side effects. Subjects were started on venlafaxine extended-release 37.5 mg po q day for the first 4 days. The dose was then increased by 37.5 mg increments every 4 days to a target of 225 mg/day (reached by the end of 3 weeks) as tolerated. Subjects then remained on that dose until week 8, at which time, if they had not had significant improvement in compulsive hoarding symptoms, the dose was increased to 300 mg po q day as tolerated for weeks 9–12. Dosages could be maintained or reduced if a subject could not tolerate higher doses. No other psychotropic medications were permitted during the study. Subjects also could not receive cognitive-behavioral therapy (CBT), assistance from professional organizers or cleaning crews, or other interventions from third parties during the treatment period.

Statistical Analyses

The data were first statistically screened for distributional properties, outliers, and missing values. No variables were rejected by this process. Because rating scale data were not normally distributed, non-parametric Wilcoxon signed-rank tests were conducted on pre- and post-treatment standardized symptom rating scale scores. Paired samples t-tests were conducted on pre- and post-treatment SI-R and UHSS component factor scores. To determine whether pre-treatment hoarding severity was associated with treatment response, Spearman’s rho correlations between age, final venlafaxine extended-release dose, baseline symptom rating scale scores, baseline UHSS and SI-R factor scores, and pre- to post-treatment changes on the UHSS and SI-R were performed.

Results

Of the 24 subjects, seven subjects had comorbid major depressive disorder (MDD), five had compulsive buying, four had comorbid attention deficit/hyperactivity disorder (ADHD), three had comorbid generalized anxiety disorder (GAD), and one had comorbid social anxiety disorder. Although we did not attempt to exclude subjects with comorbid non-

hoarding OCD, only one subject in this study met diagnostic criteria for non-hoarding OCD, and four had subclinical OC symptoms. None had hoarding behavior related to other, “typical” OCD obsessions. Baseline, pre-treatment hoarding symptom severity was in the moderate to severe range, with a mean UHSS score of 24.4 ± 3.9 and a mean SI-R score of 68.8 ± 9.9 .

23 of the 24 subjects (96%) completed treatment with venlafaxine extended-release for 12 weeks, and one dropped out of the study after ten weeks because she moved out of state. No patients dropped out of the study because of side effects or lack of efficacy. The mean final dose was 204 ± 72 mg/day. Twenty of the 23 patients were able to tolerate at least 150 mg/day, sixteen tolerated at least 225 mg/day, and four reached a final dose of 300 mg/day.

Compulsive hoarding symptoms improved significantly. Mean UHSS score declined by 36% ($Z = -4.20$, $p < .0001$), and mean SI-R score decreased 32% ($Z = -4.02$, $p < .001$). The effect sizes for reduction in hoarding symptom severity with venlafaxine extended-release treatment were large (1.98 for the UHSS, 1.68 for the SI-R). Significant, pre- to post-treatment declines were found for all three UHSS component factors ($t = 10.76$, $df = 22$, $p < .001$ for associated features & functional impairment; $t = 5.01$, $df = 22$, $p < .001$ for core symptoms; and $t = 11.69$, $df = 22$, $p < .001$ for clutter & social impairment). All three SI-R component factors also showed significant, pre- to post-treatment improvements ($t = 6.63$, $df = 22$, $p < .001$ for clutter; $t = 7.37$, $df = 22$, $p < .001$ for difficulty discarding; and $t = 6.92$, $df = 22$, $p < .001$ for excessive acquisition). Sixteen of the 23 completers (70%) were classified as responders to treatment, based on 30% reduction of UHSS and SI-R scores, as well as a rating of at least “much improved” on the CGI-I.

Depression, anxiety, OCD symptoms, and overall functioning also improved significantly, with a 48% decline in mean HDRS score ($Z = -3.34$, $p = .001$), 43% decrease in mean HAM-A score ($Z = -3.54$, $p < .001$), 39% decline in mean YBOCS score ($Z = -4.03$, $p < .001$), and a 19% increase in mean GAS score ($Z = -4.20$, $p < .001$).

Improvement in hoarding severity was not significantly correlated with pre-treatment UHSS, SI-R, HDRS, HAM-A, YBOCS, or GAS scores, nor with dose of venlafaxine extended-release. However, there was a significant negative correlation between age and improvement on the SI-R ($\rho = -.53$, $p = .009$), and a trend toward a significant negative correlation between age and improvement on the UHSS ($\rho = -.37$, $p = .08$), indicating that higher patient age was associated with less improvement in hoarding symptoms with treatment. Age was also significantly, negatively correlated with improvement in the UHSS core symptoms factor ($\rho = -.51$, $p = .02$). As expected, pre-treatment UHSS and SI-R scores were strongly correlated ($\rho = .76$, $p < .001$), as were the pre- to post-treatment changes in UHSS and SI-R scores ($\rho = .69$, $p < .001$).

Discussion

To our knowledge, this is the first study to have prospectively and quantitatively assessed response to standardized medication treatment of patients with Hoarding Disorder with specific measures of pre- and post-treatment hoarding symptom severity in all patients. The

results of this open trial suggest that venlafaxine extended-release may be quite effective for treatment of Hoarding Disorder, with a large effect size, and is well tolerated in these patients. The categorical responder rate (70%) and the effect sizes for reduction in hoarding symptom severity after treatment with venlafaxine extended-release (1.98 on the UHSS, 1.68 on the SI-R) were quite large, and they compare favorably with the effect sizes of many pharmacotherapy trials for OCD (Soomro et al. 2008). Moreover, significant, pre- to post-treatment decreases were seen on all SI-R and UHSS component factors, indicating that treatment with venlafaxine extended-release resulted in broad improvements in all major components of the compulsive hoarding syndrome – difficulty discarding, excessive acquisition, clutter, associated features, and functional impairment. There were no dropouts due to side effects or lack of efficacy. Taken together, the results of the current study of venlafaxine extended-release and the prior study of paroxetine treatment for compulsive hoarding (Saxena et al. 2007) indicate that the “conventional wisdom” that compulsive hoarding does not respond well to SRI treatment is wrong. SSRI/SNRI medications appear to be as effective for patients with Hoarding Disorder as for non-hoarding OCD patients. Randomized, double-blind, placebo-controlled trials of venlafaxine extended-release for Hoarding Disorder are now warranted.

Symptom improvement from pharmacotherapy of compulsive hoarding compares quite favorably with that resulting from CBT. In published CBT trials, improvement in compulsive hoarding symptoms, measured by decline in mean SI-R score, has ranged from 10–30% for group CBT (Steketee et al. 2000, Muroff et al. 2009, Muroff et al. 2010, Gilliam et al. 2011, Muroff et al. 2012) to 27–28% for individual CBT (Tolin et al. 2007, Steketee et al. 2010). However, in the present study, treatment with venlafaxine extended-release resulted in a 32% mean improvement on the SI-R and 36% on the UHSS, while in the previous paroxetine study, mean symptom improvement was 31% for completers and 24% for the entire sample in an intent to treat analysis (Saxena et al. 2007). The effect sizes for reduction in hoarding severity with venlafaxine extended-release treatment in the present study were considerably larger than those found in the prior studies of CBT for hoarding with similar treatment duration (twelve weeks), and similar to those found in recent studies of facilitated support group treatment of hoarding (Frost et al. 2011a, Frost et al. 2012). Larger improvements have been found using the Hoarding Rating Scale (HRS - Tolin et al. 2010b) and longer durations of treatment; Steketee et al. (2010) found a 39% decline in HRS scores after 26 weeks of individual CBT for compulsive hoarding. The improvements in depression and anxiety symptoms with venlafaxine extended-release in this study also were larger than those achieved in most prior studies of CBT or facilitated support group treatment of hoarding.

Further, pharmacotherapy may lead to faster improvement in compulsive hoarding symptoms than CBT. In both the venlafaxine extended-release and paroxetine trials, significant improvement was found after only twelve weeks of treatment, whereas the individual and group CBT trials required up to 26 weeks to achieve at least 25% mean improvement on the SI-R and comparable effect sizes. Future trials of CBT or other therapies should control for the significant effects of medication treatment on hoarding symptoms, and should require that medications not be started or adjusted during the

treatment period; most prior CBT and support group studies have failed to control for potential medication treatment effects.

No study has yet compared CBT and pharmacotherapy for compulsive hoarding directly. The combination of anti-obsessional pharmacotherapy and CBT for Hoarding Disorder may be more effective than either treatment alone, as has been found in systematic meta-analyses for major depression (Pampallona et al. 2004), panic disorder and agoraphobia (van Balkom et al. 1997, Furukawa et al. 2007), and in some studies of OCD (Hohagen et al. 1998; Pediatric OCD Treatment Study Team 2004).

Age was the only pre-treatment variable found to correlate significantly with response to venlafaxine extended-release in this study. Older age was significantly correlated with less improvement in hoarding symptoms, as measured by the SI-R (with a trend towards a significant correlation with less improvement on the UHSS, as well). This finding is consistent with previous findings of poorer response to CBT in elderly hoarders, compared to younger and middle-aged compulsive hoarders (Ayers et al. 2011). However, to our knowledge, age has not been reported to be a significant correlate or predictor of treatment response in prior treatment studies of Hoarding Disorder.

Limitations

This study is limited by its open-label design and relatively small sample size. Large, randomized, double-blind, placebo-controlled studies will be needed to establish the efficacy of venlafaxine extended-release treatment for Hoarding Disorder. The study population consisted only of patients requesting treatment for compulsive hoarding, and who were free from many confounds, such as other psychotropic medications, concurrent psychotherapies, and many comorbid neuropsychiatric disorders. Thus, it is possible that the results of this study might not be generalizable to the broader population of compulsive hoarders with various comorbid psychiatric disorders and variable motivation for treatment. However, similar limitations are present in most clinical drug efficacy trials. The study did include subjects with several comorbid psychiatric disorders - MDD, ADHD, GAD, social anxiety disorder, compulsive buying, and OCD – that have been found to commonly be comorbid with Hoarding Disorder (Frost et al. 2011b), which supports its generalizability. The prevalence of comorbid psychiatric disorders in our subject sample was similar to those reported in a large sample by Frost et al (2011b), with MDD, compulsive buying, ADHD, and GAD being the most frequent. Unfortunately, the sample size was too small to assess the influence of these comorbidities on treatment response in this study. Another limitation was that we did not assess symptom severity more frequently during the 12 week treatment period, so we were not able to analyze the speed or trajectory of symptom improvement quantitatively. Future studies may need to rate symptom severity every one to two weeks to determine the onset and pace of clinical response to treatment. Another important limitation was that no home visits were done to assess clutter volume or hazards in the patients' living spaces.

Nevertheless, this study also had several strengths that add to the importance of its results. All subjects were prospectively diagnosed with valid diagnostic instruments and assessed with specific symptom rating scales before and after standardized treatment. Both clinician-

rated and self-report symptom rating scales were used, an important issue in assessing symptoms of a disorder known to be frequently characterized by poor insight (Pertusa et al. 2010, Neziroglu et al. 2012). The subject sample had moderate to severe symptoms at baseline, with pre-treatment UHSS scores (24.4 ± 3.9) similar to those found in the paroxetine study (Saxena et al. 2007), and SI-R scores (68.8 ± 9.9) that were slightly higher than those of multiple prior samples of compulsive hoarding subjects in CBT and support group studies, which have ranged from 59–67 (Steketee et al. 2000, Tolin et al. 2007, Muroff et al. 2009, Muroff et al. 2010, Steketee et al. 2010, Gilliam et al. 2011, Frost et al. 2011, Frost et al. 2012, Muroff et al. 2012). Both self-report and clinician-administered hoarding severity rating scales demonstrated clinically and statistically significant improvements in hoarding symptom severity with treatment. The average age (51.8 ± 8.1) and gender distribution (88% female) of the subject sample was also very similar to those of prior studies of compulsive hoarding patients. Thus, the sample appears fairly representative of Hoarding Disorder patients in other clinical and research settings.

This present study also avoided any potential confound from other potentially active treatments. All other psychotropic drugs besides venlafaxine were disallowed, as were CBT and any other psychotherapy that addressed compulsive hoarding symptoms, as well as any assistance from professional organizers or cleaning crews, or other interventions from third parties during the treatment period. Thus, the significant clinical improvements in hoarding severity and comorbid conditions can reasonably be attributed to the effect of treatment with venlafaxine extended-release, to the extent possible in an open-label trial.

Moreover, the extremely low dropout rate and significant improvement in hoarding symptom severity, comorbid symptoms, and overall functioning suggest that extended-release venlafaxine is well tolerated and may be effective for treatment of Hoarding Disorder.

Acknowledgments

Sources of Funding

This study was funded in part by NIMH R01 MH069433 (Saxena). Extended-release venlafaxine (Effexor XR) was provided by Pfizer, Inc. (formerly by Wyeth Pharmaceuticals). No other funding was provided.

References

- Albert U, Aguglia E, Maina G, Bogetto F. Venlafaxine versus clomipramine in the treatment of obsessive-compulsive disorder: a preliminary single-blind, 12-week, controlled study. *J Clin Psychiatry*. 2002; 63(11):1004–1009. [PubMed: 12444814]
- Alonso P, Menchon JM, Pifarre J, Mataix-Cols D, Torres L, Salgado P, et al. Long-term follow-up and predictors of clinical outcome in obsessive-compulsive patients treated with serotonin reuptake inhibitors and behavioral therapy. *J Clin Psychiatry*. 2001; 62:535–540. [PubMed: 11488364]
- Ayers CR, Saxena S, Golshan S, Wetherell JL. Age at onset and clinical features of late life compulsive hoarding. *Int J Geriatr Psychiatry*. 2010; 25:142–149. [PubMed: 19548272]
- Ayers CR, Wetherell JL, Golshan S, Saxena S. Cognitive-behavioral therapy for geriatric compulsive hoarding. *Behav Res Ther*. 2011; 49(10):689–694. [PubMed: 21784412]
- Ayers CR, Saxena S, Espejo E, Twamley EW, Granholm E, Wetherell JL. Novel treatment for geriatric hoarding disorder: An open trial of cognitive rehabilitation paired with behavior therapy. *Am J Geriatr Psychiatry*. 2013a Jul 3. Epub ahead of print.

- Ayers CR, Ly P, Howard I, Mayes T, Porter B, Iqbal Y. Hoarding severity predicts functional disability in late-life hoarding disorder patients. *Int J Geriatr Psychiatry*. 2013b Epub ahead of print.
- Black DW, Monahan P, Gable J, Blum N, Clancy G, Baker P. Hoarding and treatment response in non-depressed subjects with obsessive-compulsive disorder. *J Clin Psychiatry*. 1998; 59:420–425. [PubMed: 9721822]
- Bloch MH, McGuire J, Landeros-Weisenberger A, Leckman JF, Pittenger C. Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. *Mol Psychiatry*. 2010; 15(8): 850–855. [PubMed: 19468281]
- Denys D, van der Wee N, van Megen HJ, Westenberg HG. A double blind comparison of venlafaxine and paroxetine in obsessive-compulsive disorder. *J Clin Psychopharmacol*. 2003; 23(6):568–575. [PubMed: 14624187]
- Dimauro J, Tolin DF, Frost RO, Steketee G. Do people with hoarding disorder under-report their symptoms? *J Obsessive Compuls Relat Disord*. 2013; 2(2):130–136. [PubMed: 23524977]
- Endicott J, Spitzer RL, Fleiss JL, Cohen J. The global assessment scale. A procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976; 41:586–601.
- Erzegovesi S, Cavallini MC, Cavedini P, Diaferia G, Locatelli M, Bellodi L. Clinical predictors of drug response in obsessive-compulsive disorder. *J Clin Psychopharm*. 2001; 21:488–492.
- Ferrao YA, Shavitt RG, Bedin NR, de Mathis ME, Carlos Lopes A, Fontenelle LF, et al. Clinical features associated to refractory obsessive-compulsive disorder. *J Affect Disord*. 2006; 94:199–209. [PubMed: 16764938]
- First, MB.; Spitzer, RL.; Williams, JBW.; Gibbon, M. Structured clinical interview for DSM-IV (SCID). Washington, DC: American Psychiatric Association; 1995.
- Frost RO, Gross RC. The hoarding of possessions. *Behav Res Ther*. 1993; 31:367–381. [PubMed: 8512538]
- Frost R, Hartl T. A cognitive-behavioral model of compulsive hoarding. *Behav Res Ther*. 1996; 34:341–350. [PubMed: 8871366]
- Frost RO, Hristova V. Assessment of hoarding. *J Clin Psychol*. 2011; 67(5):456–466. [PubMed: 21351103]
- Frost RO, Steketee G, Williams LF, Warren R. Mood, personality disorder symptoms, and disability in obsessive compulsive hoarders: a comparison with clinical and non-clinical controls. *Behav Res Ther*. 2000; 38:1071–1081. [PubMed: 11060936]
- Frost RO, Steketee G, Grisham J. Measurement of compulsive hoarding: saving inventory-revised. *Behav Res Ther*. 2004; 42:1163–1182. [PubMed: 15350856]
- Frost RO, Tolin DF, Steketee G, Fitch KE, Selbo-Bruns A. Excessive acquisition in hoarding. *J Anxiety Disord*. 2009; 23(5):632–639. [PubMed: 19261435]
- Frost RO, Pekareva-Kochergina A, Maxner S. The effectiveness of a biblio-based support group for hoarding disorder. *Behav Res Ther*. 2011a; 49(10):628–634. [PubMed: 21831357]
- Frost RO, Steketee G, Tolin DF. Comorbidity in hoarding disorder. *Depress Anxiety*. 2011b; 28(10): 876–884. [PubMed: 21770000]
- Frost RO, Ruby D, Shuer LJ. The buried in treasures workshop: waitlist control trial of facilitated support groups for hoarding. *Behav Res Ther*. 2012; 50(11):661–667. [PubMed: 22982080]
- Furukawa TA, Watanabe N, Churchill R. Combined psychotherapy plus antidepressants for panic disorder with or without agoraphobia. *Cochrane Database Systc Rev*. 2007; 1:CD004364.
- Gilliam CM, Norberg MM, Villavicencio A, Morrison S, Hannan SE, Tolin DF. Group cognitive-behavioral therapy for hoarding disorder: an open trial. *Behav Res Ther*. 2011; 49(11):802–807. [PubMed: 21925643]
- Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, et al. The Yale-Brown Obsessive Compulsive Scale I. Development, use, and reliability. *Arch Gen Psychiatry*. 1989; 46:1006–1011. [PubMed: 2684084]
- Grisham JR, Frost RO, Steketee G, Kim HJ, Hood S. Age of onset of compulsive hoarding. *J Anxiety Disord*. 2006; 20:675–686. [PubMed: 16112837]
- Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol*. 1959; 32:50–55. [PubMed: 13638508]

- Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960; 23:56–62. [PubMed: 14399272]
- Hohagen F, Winkelmann G, Rasche-Rüchle H, Hand I, König A, Münchau N, et al. Combination of behaviour therapy with fluvoxamine in comparison with behaviour therapy and placebo. Results of a multicentre study. *Br J Psychiatry Suppl*. 1998; 35:71–78. [PubMed: 9829029]
- Hollander E, Friedberg J, Wasserman S, Allen A, Birnbaum M, Koran LM. Venlafaxine in treatment-resistant obsessive-compulsive disorder. *J Clin Psychiatry*. 2003; 64(5):546–550. [PubMed: 12755657]
- Ibor JJ, Carrasco JL, Prieto R, García-Calvo C. Ceres Study Group. Effectiveness and safety of venlafaxine extended release in elderly depressed patients. *Arch Gerontol Geriatr*. 2008; 46(3): 317–326. [PubMed: 17617478]
- Iervolino AC, Perroud N, Fullana MA, Guipponi M, Cherkas L, Collier DA, et al. Prevalence and heritability of compulsive hoarding: a twin study. *Am J Psychiatry*. 2009; 166(10):1156–1161. [PubMed: 19687130]
- Landeros-Weisenberger A, Bloch MH, Kelmendi B, Wegner R, Nudel J, Dombrowski P, et al. Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder. *J Affect Disord*. 2010; 121(1–2):175–179. [PubMed: 19577308]
- Lochner C, du Toit PL, Van Kradenburg J, Stein DJ. Expanded SCID for OCD Spectrum Disorders (SCID-OCD), Version 7. 2005 Unpublished.
- Marazziti D. Venlafaxine treatment of obsessive-compulsive disorder: case reports. *CNS Spectr*. 2003; 8(6):421–422. [PubMed: 12858131]
- Mataix-Cols D, Rauch SL, Manzo PA, Jenike MA, Baer L. Use of factor-analyzed symptom dimensions to predict outcome with serotonin reuptake inhibitors and placebo in the treatment of obsessive-compulsive disorder. *Am J Psychiatry*. 1999; 156:1409–1416. [PubMed: 10484953]
- Mataix-Cols D, Frost RO, Pertusa A, Clark LA, Saxena S, Leckman JF, et al. Hoarding disorder: a new diagnosis for DSM-V? *Depress Anxiety*. 2010; 27:556–572. [PubMed: 20336805]
- Mataix-Cols D, Billotti D, Fernández de la Cruz L, Nordsletten AE. The London field trial for hoarding disorder. *Psychol Med*. 2013; 43(4):837–847. [PubMed: 22883395]
- Maze D, Shahal B, Aviv A, Zemishlani H, Barak Y. A randomized, single-blind, comparison of venlafaxine with paroxetine in elderly patients suffering from resistant depression. *Int Clin Psychopharmacol*. 2007; 22(6):371–375. [PubMed: 17917556]
- Mueller A, Mitchell JE, Crosby RD, Glaesmer H, de Zwaan M. The prevalence of compulsive hoarding and its association with compulsive buying in a German population-based sample. *Behav Res Ther*. 2009; 47:705–709. [PubMed: 19457476]
- Muroff J, Steketee G, Rasmussen J, Gibson A, Bratilis C, Sorrentino C. Group cognitive and behavioral treatment for compulsive hoarding: a preliminary trial. *Depress Anxiety*. 2009; 26(7): 634–640. [PubMed: 19569229]
- Muroff J, Steketee G, Himle J, Frost RO. Delivery of internet treatment for compulsive hoarding (D.I.T.C.H.). *Behav Res Ther*. 2010; 48(1):79–85. [PubMed: 19800051]
- Muroff J, Steketee G, Bratilis C, Ross A. Group cognitive and behavioral therapy and bibliotherapy for hoarding: a pilot trial. *Depress Anxiety*. 2012; 29(7):597–604. [PubMed: 22447579]
- Neziroglu F, Weissman S, Allen J, McKay D. Compulsive hoarders: how do they differ from individuals with obsessive compulsive disorder? *Psychiatry Res*. 2012; 200(1):35–40. [PubMed: 22748189]
- Nordsletten AE, Reichenberg A, Hatch SL, de la Cruz LF, Pertusa A, Hotopf M, Mataix-Cols D. Epidemiology of hoarding disorder. *Br J Psychiatry*. 2013; 203(6):445–452. [PubMed: 24158881]
- Pampallona S, Bollini P, Tibaldi G, Kupelnick B, Munizza C. Combined pharmacotherapy and psychological treatment for depression: a systematic review. *Arch Gen Psychiatry*. 2004; 61(7): 714–719. [PubMed: 15237083]
- Pediatric OCD Treatment Study (POTS) Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA*. 2004; 292(16):1969–1976. [PubMed: 15507582]

- Pertusa A, Frost RO, Fullana MA, Samuels J, Steketee G, Tolin D, et al. Refining the diagnostic boundaries of compulsive hoarding: a critical review. *Clin Psychol Rev.* 2010; 30(4):371–386. [PubMed: 20189280]
- Salomoni G, Grassi M, Mosini P, Riva P, Cavedini P, Bellodi L. Artificial neural network model for the prediction of obsessive-compulsive disorder treatment response. *J Clin Psychopharmacology.* 2009; 29:343–349.
- Samuels J, Bienvenu OJ, Riddle MA, Cullen BA, Grados MA, Liang KY, et al. Hoarding in obsessive-compulsive disorder: results from a case-control study. *Behav Res Ther.* 2002; 40:517–528. [PubMed: 12043707]
- Samuels JF, Bienvenu OJ 3rd, Pinto A, Fyer AJ, McCracken JT, Rauch SL, et al. Hoarding in obsessive-compulsive disorder: results from the OCD Collaborative Genetics Study. *Behav Res Ther.* 2007; 45(4):673–686. [PubMed: 16824483]
- Samuels JF, Bienvenu OJ, Grados MA, Cullen B, Riddle MA, Liang KY, et al. Prevalence and correlates of hoarding behavior in a community-based sample. *Behav Res Ther.* 2008; 46:836–844. [PubMed: 18495084]
- Saxena S. Is compulsive hoarding a genetically and neurobiologically discrete syndrome? Implications for diagnostic classification. *Am J Psychiatry.* 2007; 164(3):380–384. [PubMed: 17329459]
- Saxena S. Pharmacotherapy of compulsive hoarding. *J Clin Psychol.* 2011; 67:477–484. [PubMed: 21404273]
- Saxena S, Maidment KM, Vapnik T, Golden G, Rishwain T, Rosen RM, et al. Obsessive-compulsive hoarding: symptom severity and response to multi-modal treatment. *J Clin Psychiatry.* 2002; 63(1):21–27. [PubMed: 11838621]
- Saxena S, Brody AL, Maidment KM, Baxter LR Jr. Paroxetine treatment of compulsive hoarding. *J Psychiatric Res.* 2007; 41:481–487.
- Saxena S, Ayers CR, Maidment KM, Vapnik T, Wetherell JL, Bystritsky A. Quality of life and functional impairment in compulsive hoarding. *J Psychiatr Res.* 2011; 45(4):475–480. [PubMed: 20822778]
- Saxena, S.; Maidment, KM.; Ayers, CR. The UCLA Hoarding Severity Scale: Development and validation. Presented at International OCD Foundation 20th Annual Conference; Atlanta, GA. July 20, 2013; 2013.
- Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry.* 1998; 59(Suppl 20):22–33. [PubMed: 9881538]
- Shetti CN, Reddy YCJ, Kandavel T, Kashyap K, Singiseti S, Hiremath AS, et al. Clinical predictors of drug nonresponse in obsessive-compulsive disorder. *J Clin Psychiatry.* 2005; 66:1517–1523. [PubMed: 16401151]
- Soomro GM, Altman D, Rajagopal S, Oakley-Browne M. Selective serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD). *Cochrane Database Syst Rev.* 2008; 1:CD001765. [PubMed: 18253995]
- Staab JP, Evans DL. Efficacy of venlafaxine in geriatric depression. *Depress Anxiety.* 2000; 12(Suppl 1):63–68. [PubMed: 11098416]
- Stein DJ, Andersen EW, Overo KF. Response of symptom dimensions in obsessive-compulsive disorder to treatment with citalopram or placebo. *Rev Bras Psiquiatr.* 2007; 29:303–307. [PubMed: 18200396]
- Stein DJ, Carey PD, Lochner C, Seedat S, Fineberg N, Andersen EW. Escitalopram in obsessive-compulsive disorder: response of symptom dimensions to pharmacotherapy. *CNS Spectr.* 2008; 13:492–498. [PubMed: 18567973]
- Steketee G, Frost R. Compulsive hoarding: current status of the research. *Clin Psychol Rev.* 2003; 23:905–927. [PubMed: 14624821]
- Steketee G, Frost RO, Wincze J, Greene K, Douglass H. Group and individual treatment of compulsive hoarding: A pilot study. *Behav Cog Psychotherapy.* 2000; 28:259–268.
- Steketee G, Frost RO, Tolin DF, Rasmussen J, Brown TA. Waitlist-controlled trial of cognitive behavior therapy for hoarding disorder. *Depress Anxiety.* 2010; 27:476–484. [PubMed: 20336804]

- Timpano KR, Exner C, Glaesmer H, Rief W, Keshaviah A, Brähler E, et al. The epidemiology of the proposed DSM-5 hoarding disorder: exploration of the acquisition specifier, associated features, and distress. *J Clin Psychiatry*. 2011; 72:780–786. [PubMed: 21733479]
- Tolin DF, Abramowitz JS, Diefenbach GJ. Defining response in clinical trials for obsessive-compulsive disorder: a signal detection analysis of the Yale-Brown obsessive compulsive scale. *J Clin Psychiatry*. 2005; 66(12):1549–1557. [PubMed: 16401156]
- Tolin DF, Frost RO, Steketee G. An open trial of cognitive-behavioral therapy for compulsive hoarding. *Behav Res Ther*. 2007; 45:1461–1470. [PubMed: 17306221]
- Tolin DF, Frost RO, Steketee G, Gray KD, Fitch KE. The economic and social burden of compulsive hoarding. *Psychiatry Res*. 2008a; 160(2):200–211. [PubMed: 18597855]
- Tolin DF, Frost RO, Steketee G, Fitch KE. Family burden of compulsive hoarding: results of an internet survey. *Behav Res Ther*. 2008b; 46(3):334–344. [PubMed: 18275935]
- Tolin DF, Meunier SA, Frost RO, Steketee G. Course of compulsive hoarding and its relationship to life events. *Depress Anxiety*. 2010a; 27(9):829–838. [PubMed: 20336803]
- Tolin DF, Frost RO, Steketee G. A brief interview for assessing compulsive hoarding: the Hoarding Rating Scale-Interview. *Psychiatry Res*. 2010b; 178(1):147–152. [PubMed: 20452042]
- van Balkom AJ, Bakker A, Spinhoven P, Blaauw BM, Smeenk S, Ruesink B. A meta-analysis of the treatment of panic disorder with or without agoraphobia: a comparison of psychopharmacological, cognitive-behavioral, and combination treatments. *J Nerv Ment Dis*. 1997; 185(8):510–516. [PubMed: 9284865]
- Winsberg M, Cassic K, Koran L. Hoarding in obsessive-compulsive disorder: a report of 20 cases. *J Clin Psychiatry*. 1999; 60(9):591–597. [PubMed: 10520977]

Table 1

Symptom Rating Scale Scores Before and After Treatment

Symptom Rating Scale	Pre-Treatment Score	Post-Treatment Score	Wilcoxon signed-rank test	
			Z	p
UHSS	24.4 +/- 3.9	15.5 +/- 4.9	-4.20	<.001
SI-R	68.8 +/- 9.9	46.5 +/- 15.4	-4.02	<.001
HDRS (17)	11.0 +/- 6.3	5.7 +/- 3.5	-3.34	.001
HAM-A	11.0 +/- 5.6	6.3 +/- 3.7	-3.54	<.001
YBOCS	22.3 +/- 4.2	13.7 +/- 5.5	-4.03	<.001
GAS	52.9 +/- 6.0	63.0 +/- 6.4	-4.20	<.001

UHSS = UCLA Hoarding Severity Scale; SI-R = Saving Inventory-Revised; HDRS = Hamilton Depression Rating Scale; HAM-A = Hamilton Anxiety Scale; YBOCS = Yale-Brown Obsessive-Compulsive Scale; GAS = Global Assessment Scale.