Nefazodone and the Treatment of Nonparaphilic Compulsive Sexual Behavior: A Retrospective Study

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Background: Recent reports suggest that individuals with nonparaphilic compulsive sexual behavior can be treated pharmacologically with selective serotonin reuptake inhibitors (SSRIs) to control sexual obsessions and compulsions. However, these medications have produced sexual side effects that may limit long-term use, particularly as individuals strive to reestablish healthy sexual relationships. Nefazodone is an antidepressant that is not associated with the sexual side effects of other SSRIs. We examined retrospective data from our clinic to investigate whether nefazodone has utility in the treatment of nonparaphilic compulsive sexual behavior.

Method: Fourteen subjects who met DSM-IV criteria for sexual disorder NOS as well as criteria used by our research group for nonparaphilic compulsive sexual behavior and who had been treated with nefazodone were selected from patient charts at our clinic. The treating physician abstracted information from the charts regarding comorbid psychiatric conditions, medication, dosage, treatment response, and side effects.

Results: In this study, the mean dosage of nefazodone was 200 mg/day. Of the subjects who remained on long-term nefazodone therapy, 6 (55%) reported good control of sexual obsessions and compulsions, and 5 (45%) reported a remission of sexual obsessions and compulsions.

Conclusion: Results from this preliminary retrospective study suggest that nefazodone decreases the frequency of sexual obsessions and compulsions but does not produce the undesired sexual side effects caused by SSRI treatment.

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In recent years, there has been a growing interest in the study of nonparaphilic compulsive sexual behavior. Other terms have been used to describe this disorder, including *compulsive sexuality, sexual addiction, paraphilia-related disorders, hyperphilia,* and *hypersexuality*. Our research group uses the term *nonparaphilic compulsive sexual behavior* and defines the disorder as one in which the individual has intense sexually arousing fantasies, urges, and associated sexual behaviors that cause significant distress or impairment for a period of greater than 6 months. Unlike the paraphilias, the sexual fantasies involve culturally sanctioned aspects of normative sexual urges and behaviors. While the correct terminology and definition of this disorder remain a matter of some debate, there has been increasing clinical recognition of this disorder. Some studies estimate that 3% to 5% of the general population has this disorder.[1–4]

Nonparaphilic compulsive sexual behavior has features similar to paraphilias. Paraphilias are defined in DSM-IV as involving intense sexually arousing fantasies and urges with associated sexual behaviors that cause significant stress or impairments in functioning for periods of greater than 6 months.[5] Unlike nonparaphilic compulsive sexual behaviors, paraphilias involve fantasies and urges that are socially deviant. Recent reports support the hypothesis that paraphilias involve serotonin dysregulation.[6,7] Although paraphilias are seen as impulse-control disorders, they also show similarities to obsessive-compulsive disorder (OCD). Individuals with nonparaphilic compulsive sexual behavior have recurrent, intrusive fantasies and engage in associated behaviors in a compulsive manner. Associated behaviors include compulsive cruising for potential sex partners, multiple partners, compulsive autistic fixation, compulsive love affairs, and compulsive sexuality in relationships.[7] These behaviors, however, are not always perceived as ego-dystonic, as in classical OCD.

Given the efficacy of selective serotonin reuptake inhibitors (SSRIs) in the treatment of obsessive-compulsive disorder, obsessive-compulsive spectrum disorders, and impulse-control disorders, increased attention has been focused on the use of SSRIs in the treatment of paraphilias. Recent open-label studies have indicated that SSRIs may be efficacious in the treatment of paraphilias.[8–12]

Given the promising results of SSRI treatment of paraphilias, there has been a growing interest in the use of SSRIs (e.g., fluoxetine, sertraline) in the treatment of individuals with nonparaphilic compulsive sexual behavior.[8–11] These open-label studies have not fully addressed whether positive responses to SSRIs are due to a decrease in the underlying obsessive sexual thoughts or to the sexual side effects (decreased libido, delayed ejaculation, anorgasmia) associated with these medications.

Nefazodone is a phenylpiperazine antidepressant with mixed noradrenergic/serotonergic reuptake inhibitor effects and is a competitive antagonist at the serotonin-2 (5-HT_2) receptor subtype. Antagonism of 5-HT_2 receptors has been associated with a lower incidence of sexual side effects in comparison with standard SSRIs.[13] This lower incidence of sexual side effects may be related to the specific effects of 5-HT_2 receptors on adrenergic mechanisms that mediate orgasm.[14]

In our clinical experience, many patients with nonparaphilic compulsive sexual behavior find SSRIs helpful in controlling their sexual obsessions and compulsions, but they have complained of the sexual side effects. These side effects can be problematic when the patients are working to establish healthy sexual relationships. Sexual side effects have often been cited as a reason for discontinuing the SSRI medication, leading to a return of sexual obsessions and compulsions.

In this study, we retrospectively reviewed the charts of individuals diagnosed with nonparaphilic compulsive sexual behavior who had been treated with nefazodone in our clinic. The treating physician selected this medication because he thought it was clinically indicated. However, nefazodone was often prescribed specifically to assess whether it would decrease sexual obsessions and compulsions without causing sexual side effects. In our retrospective review, the main question we hoped to address was whether nefazodone, like SSRIs, would be effective in the treatment of nonparaphilic compulsive sexual behavior and, secondly, whether the side effect profile would be well tolerated by this population in comparison with the SSRIs with which they had been treated.

METHOD

Subjects

The sample was obtained by selecting all of the charts of individuals who were treated for nonparaphilic compulsive sexual behavior with nefazodone from 1995 to 1997 at the Program in Human Sexuality Clinic in the Department of Family Practice and Community Health at the University of Minnesota Medical School (Minneapolis). All of the subjects presented at the clinic because of problems related to their nonparaphilic compulsive sexual behavior and were undergoing concomitant psychotherapy (i.e., individual and group therapy with a cognitive-behavioral focus) at the time of their participation in the study. The physician who was treating the individual using the diagnostic criteria described above made the diagnosis. The diagnosis of sexual disorder NOS was given to each patient in conformity with DSM-IV criteria.[11]

Procedure

The treating physician reviewed the charts to obtain the following data: (1) principal diagnosis (using our definition of nonparaphilic compulsive sexual behavior and DSM-IV criteria for sexual disorder NOS), (2) comorbid diagnosis (including paraphilias and concomitant major mental disorders), (3) reason for switch to nefazodone, (4) retrospective assessment of efficacy of nefazodone (using a rating scale of 1–4: 1 = minimal response or poor tolerance to medication, 2 = partial control of obsessive thoughts, 3 = good control of obsessive thoughts, 4 = remission of obsessive thoughts), and (5) side effects.

RESULTS

Fourteen subjects were identified using the above criteria. All 14 subjects were white men. The subjects ranged in age from 26 to 67 years, and the mean age was 45 years. All 14 subjects had been treated previously with 2 or more SSRIs (i.e., paroxetine, sertraline, fluoxetine, fluvoxamine), but were dissatisfied with these medications. Eight of the 14 subjects were switched to nefazodone because of complaints of sexual side effects (e.g., decreased sexual drive, failure to achieve erection, anorgasmia). Four patients were switched to nefazodone because the SSRIs failed to decrease recurrent and obsessive sexual thoughts. One patient was switched because an SSRI was ineffective in the treatment of depression. Finally, one subject was started on nefazodone therapy because of gastrointestinal side effects of an SSRI.

Although all of the subjects met the criteria for nonparaphilic compulsive sexual behavior as described above, 5 subjects at some point in their life history indicated a concomitant paraphilia (1, fetishism; 2, transvestic fetishism; 1, exhibitionism; 1, pedophilia). At the time that these patients presented to the clinic, this disorder was not causing clinical distress or impairment of their functioning. Nine individuals did not have a concomitant paraphilia.

Other comorbid psychiatric diagnoses were also noted and were established by clinical examination by the treating physician in combination with a review of previous diagnoses made by a referring psychologist. Nine of the 14 individuals had a mood disorder (i.e., dysthymia, depressive disorder NOS, or major depressive disorder). Three subjects with depressed mood also had anxiety disorders (i.e., a diagnosis of generalized anxiety disorder, panic disorder, or anxiety disorder NOS). One individual had generalized anxiety disorder without accompanying depressed mood. One subject was given a diagnosis of sub-

stance abuse. Four subjects did not have a comorbid Axis I diagnosis.

Three subjects discontinued nefazodone: 1 owing to poor compliance for unknown reasons and 2 owing to side effects from the nefazodone (i.e., headaches, bloating). Eleven subjects continued on long-term nefazodone treatment. The mean length of time subjects remained on nefazodone therapy was 13.4 months. The mean dose of nefazodone in this group was 200 mg/day, with a range in dosage from 50 to 400 mg/day.

The 11 patients who remained on nefazodone therapy reported a good response. The treating physician rated the efficacy of nefazodone treatment as a "3" for 6 individuals, indicating good control of recurrent, intrusive sexual thoughts. In the 5 remaining individuals, efficacy was rated as a "4," indicating a remission of recurrent and intrusive sexual thoughts. For example, 1 patient showed a complete remission in his obsessional sexual thoughts. He was able to maintain a monogamous relationship with his wife and was no longer preoccupied with thoughts of using pornography or visiting prostitutes.

The 11 individuals who remained on nefazodone therapy were also noted to have minimal side effects. None of these subjects complained of sexual side effects, even though 10 had reported sensitivity to the sexual side effects from other SSRIs. None of these subjects reported problems with headache, sedation, or abdominal discomfort, which are typical side effects associated with nefazodone. One individual had initial problems with dizziness, but this dissipated after a few weeks.

DISCUSSION

This retrospective study provides encouraging data regarding the use of nefazodone for patients with nonparaphilic compulsive sexual behavior. The 11 of 14 patients who remained on long-term nefazodone therapy showed a positive response to treatment. Six patients reported a decrease in recurrent sexual thoughts, and 5 reported a complete remission of recurrent sexual thoughts. Patients reported a low incidence of side effects to modest doses of nefazodone, and none of the subjects complained of sexual side effects.

The results of this retrospective study also suggest that nefazodone may have advantages over SSRIs in the treatment of nonparaphilic compulsive sexual behavior. Individuals with nonparaphilic compulsive sexual behavior are often particularly bothered by the sexual side effects of SSRIs in long-term use of these medications.

We were also impressed that these patients with nonparaphilic compulsive sexual behavior showed a remarkable tolerance to side effects of nefazodone therapy. It may be that individuals with nonparaphilic compulsive sexual behavior are more tolerant of the side effect profile of nefazodone than that of SSRIs (i.e., particularly as they relate to the sexual side effects) and that their response in this regard may be atypical of the population as a whole who have tried nefazodone therapy.

Limitations to this study include the small sample size, retrospective design, lack of an objective operational definition of nonparaphilic compulsive sexual behavior, lack of a thorough diagnostic evaluation of each subject, lack of an objective method to assess efficacy at predetermined intervals, and lack of a specific assessment of the ameliorative effects of concurrent psychotherapy. However, this retrospective study suggests that further investigation of the use of nefazodone in the treatment of nonparaphilic compulsive sexual behavior is warranted, especially in cases where the patient is intolerant to the sexual side effects of the SSRIs. If nefazodone is found to be effective in the treatment of nonparaphilic compulsive sexual behavior, it would suggest that the putative mechanism of action of SSRIs on nonparaphilic compulsive sexual behaviors is not merely related to sexual "side effects" mediated by enhanced 5-HT_2 neurotransmission by those drugs. Further studies of nefazodone with this population utilizing a prospective open clinical trial or a randomized double-blind, placebo-controlled methodology are needed.

Drug names: fluoxetine (Prozac), fluvoxamine (Luvox), nefazodone (Serzone), paroxetine (Paxil), sertraline (Zoloft).

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