Clinical Case Study

SSRI-INDUCED SEXUAL DYSFUNCTION TREATED WITH SILDENAFIL

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This report describes the presence of sexual dysfunction associated with selective serotonin reuptake inhibitors (SSRIs) in two male patients treated successfully with sildenafil (Viagra). The sexual dysfunction was assessed using the Arizona Sexual Experiences Scale for males (ASEX-Males; McGahuey et al. [1997: Presented at the 150th Annual Meeting of the American Psychiatric Association, May 19, 1997, San Diego, CA]). Depression and Anxiety 9:180–182, 1999. *© 1999 Wiley-Liss, Inc.*

Key words: ***sexual dysfunction; SSRI; sildenafil***

INTRODUCTION

Sexual dysfunction due to affective disorders is often complicated by antidepressant side effects. Sexual dysfunction associated with monoamine oxidase inhibitors (MAOIs) and tricyclic amines (TCAs) has been reported in the range of 23% to 40% [Harrison et al., 1986; Segraves, 1982; Lesko et al., 1982; Mitchell and Popkin, 1983; Shen and Park, 1983; Monteiro et al., 1987]. The prevalence of sexual side effects with SSRIs has been reported in the range of 6% to 75% of patients for fluoxetine [Patterson et al., 1993], sertraline [Reimherr et al., 1990], and paroxetine [Grimsley and Jann, 1992]. The variability of these rates is probably due to differences in methodology rather than indicative of a differential sexual side effect liability of the drugs themselves. Sexual side effects include decreased libido, inhibited arousal, erectile dysfunction, delayed orgasm, and anorgasmia [Ashton et al., 1997]. Strategies for treating sexual side effects of SSRIs include decreasing dosage, switching to another antidepressant [Harvey and Balon, 1995], or adjunctive medication such as cyproheptadine, yohimbine, bethanecol, bupropion, pemoline, dextroamphetamine, methylphenidate, buspirone, and amantadine [Segraves, 1994; Labbate and Pollack, 1994; Bartlik et al., 1995; Balogh et al., 1992; Michelson et al., 1998; Masand et al., 1995]. A single case report cites the efficacy of the 5-HT_3 antagonist granisetron as an augmentation to fluoxetine for resolution of sexual side effects, including decreased interest and delayed orgasm [Nelson et al., 1997]. Treatment-emergent sexual dysfunction often leads to patient distress and noncompliance [Jacobsen, 1992]. Although men (23.4%) are more likely than women (13.5%) to report sexual side effects [Ashton et al., 1997], spontaneous reports of sexual dysfunction are low enough to necessitate clinician inquiry.

We found sildenafil (Viagra) to be helpful in phenelzine-induced sexual dysfunction [Gupta et al., 1999] as measured by the Arizona Sexual Experiences Scale for Males (ASEX-M) [McGahuey et al., 1997]. The ASEX-M is a 5-item, patient-rated Likert scale that evaluates drive, arousal, erection, orgasm, and satisfaction. Scores >19, any individual item >5, or any three items = 4 indicate sexual dysfunction. To our knowledge, this is the first case series of SSRI-induced sexual dysfunction successfully treated with sildenafil.

CASE 1

WN is a 34-year-old married Caucasian male with a 4-month history of depression which included low mood, poor concentration, and despair. There was no significant past psychiatric history of hospitalization or suicide attempts, and no significant medical problems. He had been in individual psychotherapy for two years. The family history was significant for the

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mother having depression. There was a past history of alcohol abuse; however, the patient had been abstinent for one year. He did not have any problems with sexual functioning prior to medication treatment (ASEX-M = 13, done retrospectively). He was started on fluoxetine 20 mg po qd which was titrated to 40 mg po qd at 4 weeks. By his account, he received relief from the depression but experienced dizziness, sleep disturbance, and sexual dysfunction as side effects of the medication. He notes that even when the fluoxetine was decreased from 40 mg to 20 mg po qd at 8 weeks, these side effects persisted. He indicated that the dizziness and sleep disturbance were more tolerable than the sexual dysfunction (ASEX-M = 20) which was contributing to marital discord. He reported that "it's gotten very hard to get an erection" and was referred to his family physician to discuss possible use of sildenafil. He was subsequently started on sildenafil 50 mg po daily. He reported no significant change in sexual functioning with the first two doses, but noted that the third and subsequent doses were effective in increasing the ease of obtaining an erection as well as the rigidity of the erection. He had not experienced any side effects from sildenafil. He has expressed satisfaction with the medication and has noted that his marriage and his self-esteem are improved. His ASEX score on the sildenafil was 12.

CASE 2

KW, a 61-year-old married Caucasian male, had a 6-month history of depressive disorder with episodic alcohol abuse. There was no prior history of psychiatric illness or hospitalization. His medical history was significant for noninsulin-dependent diabetes mellitus which was controlled by diet. There was no history suggestive of drug or alcohol dependence. He had begun to experience depressed mood with low energy shortly after his retirement. He became anxious and his enjoyment of activities declined. He reported the symptoms to his family physician and was started on lorazepam 0.5 mg po q12h prn. The medication relieved his anxiety, but he continued to be depressed. He was then started on paroxetine 20 mg daily which was titrated up to 30 mg daily due to lack of response. At this dosage, he began to experience symptom relief and his mood returned to baseline. However, at this dosage he had difficulty in obtaining and maintaining an erection in addition to problems with ejaculation (ASEX-M = 23). He reported that he had always enjoyed a satisfying sex life in the past (ASEX-M = 17, done retrospectively). He was started on 25 mg of sildenafil orally which was ineffective. The medication was increased to 50 mg without effects. He reported that only when the dosage reached 100 mg did he note an immediate response and stated, "I haven't had an erection like that in 20 years." He cites the sildenafil and his wife's patience as being the solution to his problem. He has indicated there has been no change in the frequency of intercourse but that it is "infinitely more satisfying" now; on sildenafil, his ASEX score was 14. He states he had experienced a mild headache with the increased dosage; however, he indicates he would continue to use the sildenafil.

DISCUSSION

In this case series, the erectile dysfunction associated with SSRIs was relieved by sildenafil. Our patients did not report any clinically significant side effects such as headache (16%), flushing (10%), and dyspepsia (7%).

Sildenafil has been studied in more than 3,000 patients in the course of the clinical trials and 550 patients have been on it for greater than one year. This drug has a low discontinuation rate of 2.5% which is comparable with the placebo discontinuation rate of 2.3%. Sildenafil is a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5) [Chuang et al., 1998]. The success rate for sildenafil was 66% compared with 20% on placebo. It is important to note that sildenafil is contraindicated in patients on organic nitrates, as it may potentiate the hypotensive effects of nitrates. In a large multi-center study, sildenafil was prescribed in a flexible dose response manner with dosage escalation to 100 mg based on efficacy and tolerance. The subjects had erectile dysfunction of organic, psychogenic, or mixed causes. The mean score for men receiving the drug at 100 mg dosage was 100% higher after treatment than at baseline. The medication group reported 69% of attempts at sexual intercourse being successful compared with 22% for those receiving placebo [Goldstein et al., 1998]. The medication is generally well-tolerated. Headache, flushing, and dyspepsia are the most common adverse events.

Sildenafil should be prescribed after a thorough evaluation which includes a comprehensive medical and psychosexual history, physical examination, and focused laboratory testing. Specialized diagnostic tests such as nocturnal tumescence, biothesiometry or penile vascular studies are of value in some patients. Medical and psychosexual history, evaluation of prescribed and over-the-counter medications and physical examination remain the cornerstone of assessment. A special effort should be made to involve the patient's partner early in the evaluation process. The sexual history should focus on aspects such as erectile dysfunction, libido, ejaculation and orgasm, altered penile sensation, and partner sexual function [Boolell et al., 1996]. The medical assessment should include chronic illnesses (diabetes, anemia, renal failure), medications and recreational drugs, atherosclerotic vascular risk factors (hypertension, hypercholesterolemia, diabetes, and family history), pelvic, penile, or perenial trauma, neurological problems (multiple sclerosis, lumbosacral disc disease), past surgery (bypass surgery, radical prostatectomy), endocrine causes (hypogonadism, hyperprolactinemia, thyroid dysfunction), psychiatric illness, and sexually transmitted diseases. The psychosexual assessment should focus on self-esteem, past

and present partner relationships, and history of sexual abuse. Laboratory testing should include serum testosterone, prolactin levels, serum chemistries, thyroid stimulating hormone (TSH), and prostate-specific antigen (PSA) (Sildenafil package insert).

It is important to note that that in these two cases, sildenafil was helpful in treating SSRI-induced erectile dysfunction. In Case 1, sildenafil was not effective the first two times, but was effective the third time. The role of foreplay and adequate stimulation are important factors in conjunction with sildenafil for the alleviation of sexual dysfunction. In Case 2, the optimal dose of sildenafil was reached after titrating up to 100 mg. Although many patients benefit with 25 mg, two or three times each on 25, 50, and 100 mg should be given to ensure an adequate trial of sildenafil.

There is a need for controlled clinical trials to demonstrate the efficacy of sildenafil in treating SSRI-induced erectile dysfunction. In addition, sildenafil should be tried in the treatment of sexual dysfunction associated with other antidepressants and antipsychotic agents.

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