

## Brief Report

# Sildenafil Citrate (Viagra) for the Treatment of Erectile Dysfunction in Men With Parkinson's Disease

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**Summary:** Sildenafil citrate (Viagra) is a phosphodiesterase type V inhibitor used to treat erectile dysfunction. Ten men with idiopathic Parkinson's disease (PD) and erectile dysfunction were prescribed 50–100 mg sildenafil citrate to use in eight sexual encounters over a 2-month period. Patients underwent Unified Parkinson's Disease Rating Scale (UPDRS) evaluations and completed a Beck's Depression Inventory (BDI) and a Sexual Health Inventory-M version (SHI-M) at baseline and after 8 weeks. There was statistically significant improvement in total SHI-M scores ( $23.8 \pm 2.0$  vs  $16.6 \pm 2.8$ ;  $p = 0.01$ ),

overall sexual satisfaction ( $p = 0.03$ ), satisfaction with sexual desire ( $p = 0.04$ ), ability to achieve erection ( $p = 0.02$ ), ability to maintain erection ( $p = 0.03$ ), and ability to reach orgasm ( $p = 0.04$ ) with use of sildenafil citrate. UPDRS and BDI scores were not significantly changed. Side effects included headache in one patient during three sexual encounters. In this open-label study, sildenafil citrate significantly improved sexual function in men with PD and erectile dysfunction. **Key Words:** Parkinson's disease—Erectile dysfunction—Sildenafil citrate—Viagra—Sexual function—Impotence.

Erectile dysfunction (ED) is the inability to attain or maintain penile erection sufficient for satisfactory sexual performance.<sup>1</sup> It affects between 10 and 30 million men in the United States.<sup>2,3</sup> ED is common in men with Parkinson's disease (PD), with a reported prevalence rate of 60.7%.<sup>4–6</sup> Patients with PD also commonly report general "sexual dissatisfaction." One study of 44 patients with PD found that 81% of men and 43% of women with PD experienced diminished sexual activity as reported on a self-administered questionnaire.<sup>7</sup> Reduced sexual activity in patients with PD has been linked to disease severity, motor symptoms,<sup>6</sup> depression,<sup>8</sup> autonomic dysfunction, and antiparkinsonian medications.<sup>9</sup>

Vascular insufficiency is the most common cause of ED<sup>10</sup> in the general population. Normal erectile function depends on nitric oxide-mediated relaxation of smooth

muscle in the corpus cavernosum.<sup>11</sup> Sildenafil citrate (Viagra, Pfizer, Inc, New York, NY, USA) is the first oral agent approved by the US Food and Drug Administration to treat ED.<sup>12</sup> It is a selective inhibitor of cyclic guanosine monophosphate (cGMP) phosphodiesterase type 5, an enzyme that metabolizes cGMP in the corpus cavernosum.<sup>12</sup> Sildenafil citrate effectively improves ED in 46%–73% of men in the general population.<sup>12,13</sup>

We performed an open-label pilot study to evaluate the safety and efficacy of sildenafil citrate in men with idiopathic PD and erectile dysfunction.

## METHODS

Men with idiopathic PD and subjective complaints of erectile dysfunction were evaluated by a urologist. A 1992 National Institute of Health Consensus Panel defined ED as the inability to achieve or maintain an erection sufficient for satisfactory sexual function.<sup>1</sup> Patients who satisfied the clinical definition for ED and did not have clinically significant heart disease were treated with sildenafil citrate. Prior to treatment, each patient completed a Sexual Health Inventory Scale-M version

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(SHI-M)<sup>14</sup> and a Beck Depression Inventory (BDI).<sup>15</sup> Each patient was also evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS). Patients were prescribed 50 mg sildenafil citrate to use for eight sexual encounters during a 2-month period, and were permitted to increase the sildenafil dose to 100 mg after the first four encounters following telephone contact with the urologist and movement disorders specialist. After eight sexual encounters, patients again completed a SHI-M and a BDI and underwent UPDRS evaluation. End point and baseline scores were compared using a Wilcoxon signed rank test.

## RESULTS

Ten men with idiopathic PD and ED received sildenafil citrate. Age (mean  $\pm$  standard error of mean) was  $72.8 \pm 2.2$  years and PD duration was  $7.5 \pm 1.1$  years. All of the men were taking antiparkinsonian medications and five were experiencing motor fluctuations. Nine patients were receiving levodopa/carbidopa and one patient was on ropinirole monotherapy. In addition, five were taking adjunctive pramipexole, two were taking pergolide, and one was taking ropinirole. Two men were on amantadine and one was on tolcapone. None of the patients reported clinically relevant depression and none were receiving antidepressants. Baseline BDI score was  $5.4 \pm 0.9$  (range, 4–11).

Duration of ED was  $4.5 \pm 0.7$  years. ED did not occur prior to a diagnosis of PD in any patient. None of the patients had a history of diabetes, alcohol abuse, smoking, pelvic disease, or pelvic surgery. Two patients had a history of mild, controlled hypertension (beginning prior to PD) and took antihypertensive medication (atenolol).

Two patients had a history of hypothyroidism, were receiving thyroid supplementation, and had normal thyroid function tests. Three patients noted mild constipation, and one also reported mild lightheadedness when standing although blood pressure evaluations did not reveal orthostatic hypotension. None of the patients had additional vascular risk factors or peripheral vascular disease.

All subjects took eight doses of sildenafil citrate during the 2-month period. Four of the men increased the dose of sildenafil citrate to 100 mg after 1 month. The sildenafil citrate dose at last use was  $70 \pm 8.2$  mg.

There was statistically significant improvement in total SHI-M scores ( $23.8 \pm 2.0$  versus  $16.6 \pm 2.8$ ;  $p = 0.01$ ) with the use of sildenafil citrate (Table 1). Significant improvement was noted in overall sexual satisfaction, satisfaction with sexual desire, ability to achieve erection, ability to maintain erection, and ability to reach orgasm. There was no significant increase in level of sexual desire, number of premature ejaculations, or change in UPDRS or BDI scores.

Side effects of sildenafil citrate use were limited to headache in one patient during three sexual encounters. There were no reports of syncope or presyncope with sildenafil citrate use, and there was no worsening of orthostatic lightheadedness in the patient who had it at baseline.

## DISCUSSION

Kinsey et al. found ED to be common in men over 50 years of age.<sup>16</sup> In men over 70 years of age, the prevalence of ED may be as high as 67%.<sup>17</sup> Available treatments include vacuum-constriction devices, penile implantation prostheses, intracavernosal injections of vasodilators,<sup>18</sup> and the oral medication sildenafil citrate.

**TABLE 1.** Sexual health inventory-M version, UPDRS, and Beck depression inventory scores (mean  $\pm$  SEM) at baseline and end point

	Baseline	End point	p value
Sexual health inventory-M version*			
Total	23.8 (2.0)	16.6 (2.8)	0.01
Overall sexual satisfaction	3.8 (0.4)	2.7 (0.5)	0.03
Level of sexual desire	2.8 (0.3)	2.6 (0.4)	NS
Satisfaction with sexual desire	3.8 (0.3)	2.6 (0.5)	0.04
Ability to achieve erection	3.7 (0.4)	2.2 (0.5)	0.02
Ability to maintain erection	3.8 (0.5)	2.5 (0.5)	0.03
Premature ejaculation	2.6 (0.6)	1.7 (0.5)	NS
Ability to reach orgasm	3.3 (0.4)	2.3 (0.5)	0.04
UPDRS			
Total	21.8 (5.6)	20.8 (5.4)	NS
Motor	14.3 (3.4)	13.5 (3.4)	NS
ADL	7.5 (2.4)	7.3 (2.1)	NS
Beck's Depression Inventory	5.4 (0.9)	5.6 (0.7)	NS

UPDRS, Unified Parkinson's Disease Rating Scale; SEM, standard error of mean; ADL, activities of daily living; NS, nonsignificant.

\* All items are on a 5-point scale with lower numbers indicating better function.

The penis is comprised of two dorsal corpora cavernosa and a ventral corpus spongiosum. Erectile function depends on relaxation of corpus cavernosum smooth muscle.<sup>11,23</sup> Cavernous nerves and endothelial cells release nitric oxide (NO) in response to sexual stimuli. NO is an endothelium-derived relaxing factor in blood vessels<sup>24</sup> that stimulates the formation of cyclic-GMP by guanylate cyclase,<sup>11,23</sup> thereby causing relaxation of cavernosum smooth muscles.

Sildenafil citrate is a selective inhibitor of cyclic-GMP phosphodiesterase type 5, the primary metabolizer of cyclic GMP in the corpus cavernosum.<sup>13</sup> It improves erectile response to sexual stimuli by inhibiting cGMP hydrolysis in the corpora,<sup>25</sup> which enhances relaxation of corpus cavernosal smooth muscle. This relaxation increases blood flow into cavernosal spaces and increases intracavernosal pressure.<sup>17</sup>

Double-blind, placebo-controlled studies have found sildenafil citrate to significantly improve erectile function in men with ED.<sup>13,17</sup> The Sildenafil Study Group examined data from 10 double-blind, placebo-controlled trials and found that at doses of 50 and 100 mg, sildenafil citrate effectively improved ED in 46%–73% of men.<sup>26</sup> Sildenafil citrate has also been shown to significantly improve ED and sexual satisfaction in men with spinal cord injury between T6 and L5.<sup>25</sup>

Limited open-label studies have uncovered a high prevalence of ED in men with PD. Singer et al. compared ED in male patients with PD with healthy control subjects and found a significant difference between groups. In the PD group, 60.4% of men had ED versus 37.5% of the control group.<sup>4</sup> Another study used a self-administered questionnaire and found that 81% of men with PD reported decreased sexual activity.<sup>7</sup> Lipe et al. noted a high prevalence of sexual dysfunction in married male patients with PD, although no higher than in men with other chronic illnesses not involving the nervous system. Sexual problems were associated with disease severity and depression in both groups.<sup>8</sup> Brown et al. evaluated patients with PD and their spouses using the Gollombok Rust Inventory of Sexual Satisfaction (GRISS)<sup>19</sup> and found that more male patients than female patients reported “moderate to severe” problems with sexual function. Sixty-five percent of male patients were classified as having possible sexual dysfunction.<sup>6</sup>

The higher incidence of ED in male patients with PD compared with the general population is probably the result of autonomic dysfunction.<sup>20</sup> However, other factors may contribute. Depression is more common in patients with PD than in healthy control subjects and may cause diminished interest in sexual intercourse.<sup>21,22</sup> Fatigue, motor symptoms, and the use of antiparkinsonian

and antidepressant medications may also impair sexual function.<sup>6</sup>

We found that sildenafil citrate significantly improved sexual function in men with idiopathic PD and ED. Patients reported improvement in overall sexual satisfaction, satisfaction with sexual desire, ability to achieve erection sufficient for intercourse, ability to maintain erection, and ability to achieve an orgasm. There was no significant change in level of sexual desire. Patients reported improved satisfaction with their level of sexual desire although their actual level of sexual desire was unchanged. This may be because they were better able to satisfy their sexual desire as a result of improved sexual function. There was no increase in the number of premature ejaculations and no significant change in BDI or UPDRS scores.

Side effects of sildenafil citrate in the general population are usually mild and mostly associated with effects of vasodilation. These include headache, flushing, and small decreases in systolic and diastolic blood pressures. In one trial, roughly 2% of patients taking sildenafil citrate discontinued the medication because of adverse events, most frequently headache, flushing, and dyspepsia.<sup>27</sup> More serious cardiovascular events can occur.<sup>28</sup> The coadministration of sildenafil citrate and nitrates can produce life-threatening hypotension,<sup>28</sup> and sildenafil citrate use is contraindicated in patients receiving nitrates. Sildenafil citrate use has also been associated with ventricular arrhythmia in two men who had myocardial infarction in the past and who were not taking nitrates.<sup>29</sup> One patient with interstitial lung disease experienced severe pulmonary hemorrhage after taking 25 mg sildenafil citrate on three occasions in 2 days.<sup>30</sup> The only side effect encountered in our study was mild headache during sexual intercourse in one patient, lasting approximately 1 hour. All patients received physical examinations prior to receiving sildenafil citrate, and none had preexisting coronary artery disease, congestive heart failure, or uncontrolled hyper- or hypotension.

Sildenafil citrate may help restore sexual function in impotent men with PD. Patients having ED should undergo medical evaluation to uncover possible associated conditions that might require treatment (diabetes, thyroid disease) and to exclude contraindications to sildenafil citrate use (concurrent nitrate administration, clinically significant heart disease). Our experience suggests that sildenafil citrate is useful to improve sexual function in men with PD and ED. Larger and longer-term double-blind, placebo-controlled trials are needed to further evaluate the safety and efficacy of sildenafil citrate in impotent patients with PD.

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