

TREATMENT OF ERECTILE DYSFUNCTION AFTER RADICAL PROSTATECTOMY WITH SILDENAFIL CITRATE (VIAGRA)

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ABSTRACT

Objectives. To determine whether the response to the new oral medication, sildenafil citrate (Viagra), was influenced by the presence or absence of the neurovascular bundles, as recent reports on its success did not specify the efficacy of the drug in patients with erectile dysfunction after radical prostatectomy.

Methods. Baseline and follow-up data from 28 healthy patients presenting with erectile dysfunction after radical prostatectomy were obtained. Patients receiving any neoadjuvant/adjuvant hormones or adjuvant radiation therapy were excluded. Patients reported what their erectile status was before surgery, before sildenafil therapy, and after using a minimum of four doses of sildenafil. Both the patients and their spouses were interviewed using the Cleveland Clinic post-prostatectomy questionnaire, which includes questions about response to therapy, duration of intercourse, spousal satisfaction, side effects, and related topics. The patients were compared on the basis of the type of surgical procedure they had undergone—nerve sparing or non-nerve sparing. A positive response to sildenafil was defined as erection sufficient for vaginal penetration.

Results. Of the 15 patients who had bilateral nerve-sparing procedures, 12 (80%) had a positive response to sildenafil, with a mean duration of 6.92 minutes of vaginal intercourse. These 12 patients also reported a spousal satisfaction rate of 80%. All 12 of the responders had a positive response within the first three doses, and 10 of the 12 responded with the first or second dose. None of the 3 patients who had undergone a unilateral nerve-sparing procedure responded, nor did any of the 10 patients who had undergone a non-nerve-sparing procedure. The two most common side effects of the drug were transient headaches (39%) and abnormal color vision (11%). No patients discontinued the medication because of side effects.

Conclusions. Successful treatment of erectile dysfunction in a patient after prostatectomy with sildenafil citrate may depend on the presence of bilateral neurovascular bundles. No patient who had undergone a non-nerve-sparing procedure responded. Whether patients who undergo unilateral nerve-sparing procedures will respond to sildenafil is still unclear because of the small number of patients in our study. These findings should encourage urologists to continue to perform and perfect the nerve-sparing approach. The ability to restore potency with an oral medication after radical prostatectomy will impact our discussion with the patient on the surgical morbidity of radical prostatectomy. *UROLOGY* 52: 963–966, 1998. © 1998, Elsevier Science Inc. All rights reserved.

The recent release of sildenafil citrate (Viagra, Pfizer Pharmaceuticals), an inhibitor of phosphodiesterase 5, has dramatically changed the treatment options for patients with erectile dysfunction. Despite the current enthusiasm for this drug, there are no reports on its effectiveness in the

subgroup of patients with erectile dysfunction after radical prostatectomy. Previous publications on the efficacy of sildenafil citrate did not separate the results of this subset of patients from patients with other causes of organic impotence.¹

We report our experience using this drug in this subset of patients. We wanted to determine whether the response to sildenafil citrate was influenced by the presence or absence of the neurovascular bundles. Among those who responded, we sought to determine how many doses of sildenafil were needed for a response, the duration of intercourse, and whether the spouse reported being sat-

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Submitted: June 19, 1998, accepted (with revisions): July 17,

TABLE I. The Cleveland Clinic post-prostatectomy questionnaire

1. What was the date of your prostate surgery?
2. What type of surgery was performed (bilateral nerve-sparing, unilateral nerve-sparing, or non-nerve-sparing)?
3. Would you describe your erections before the surgery as full, partial, or none?
4. Would you describe your erections after the surgery and before starting sildenafil as full, partial, or none?
5. When did you start taking sildenafil?
6. How many times have you taken it since?
7. Did you engage in foreplay?
8. After taking sildenafil, did you have an erection adequate for vaginal penetration?
9. After taking sildenafil, how long would you estimate intercourse lasted?
10. Did you have any side effects (choose from the following: headache, dizziness, flushing, dyspepsia, nasal congestion, abnormal color vision)?
11. How many doses of sildenafil did you take before a positive response?
12. Did you take sildenafil in the correct manner as prescribed?
13. Was your spouse satisfied with the sexual intercourse?
14. Have you discontinued the drug? Why?

MATERIAL AND METHODS

We selected 28 healthy patients who had undergone radical prostatectomy who had no erections or unsatisfactory erections for this study. These patients were given a prescription for a 100-mg dose of sildenafil. Patients were instructed to take a sildenafil tablet approximately 1 hour before sexual activity per the manufacturer's instructions. Patients were told to have adequate foreplay before sexual intercourse. After taking at least four doses of the drug, the patients were asked to call in for a telephone interview to report their response. None of the 28 patients were on any concurrent form of therapy for their erectile dysfunction.

The type of surgical procedure was determined by chart review and confirmed during the telephone interview. Of the 28 patients, 10 had undergone a non-nerve-sparing procedure and 18 patients had undergone a nerve-sparing procedure. All nerve-sparing procedures and 3 of the 10 non-nerve-sparing procedures were performed by the same surgeon (C.D.Z.). Three of the 18 patients had undergone unilateral nerve-sparing procedures. None of the patients received neoadjuvant or adjuvant hormones or radiation therapy after prostatectomy.

All telephone interviews were conducted by the same person (A.K.). Table I lists the questions asked. Both patients and spouses were interviewed about the patient's presurgical and presildenafil erectile function, their use of sildenafil, their response to therapy, the duration of intercourse, side effects, and their spouse's satisfaction with sex.

Statistical methods consisted of demographic and baseline comparisons of the patients who had undergone nerve-sparing surgery with those who had undergone non-nerve-sparing procedures using Fisher's exact and Wilcoxon rank-sum tests. Fisher's exact test was used to compare the success rates in the

TABLE II. Characteristics of 28 patients with erectile dysfunction after prostatectomy before sildenafil therapy

Patient Characteristics	Nerve-Sparing Surgery (n = 18)	Non-Nerve-Sparing Surgery (n = 10)	P Value*
Age (yr)	58.78 ± 2.68	61.40 ± 2.05	0.19
Time from surgery to sildenafil (mo)	13.5 ± 2.68	11.7 ± 2.9	0.87
Presurgical erectile status (% , n)			
Full	100 (18/18)	70 (7/10)	0.18
Partial	0 (0/18)	20 (2/10)	
None	0 (0/18)	10 (1/10)	
Predrug erectile status (% , n)			
Full	0 (0/18)	0 (0/10)	0.45
Partial	28 (5/18)	10 (1/10)	
None	62 (13/18)	90 (9/10)	
Nocturnal erections present (% , n)	0 (0/18)	0 (0/10)	1.00
Able to penetrate (% , n)	0 (0/18)	0 (0/10)	1.00

Data are presented as mean ± SE unless otherwise noted.

* P < 0.05 was considered as significant; Wilcoxon rank-sum test was used.

RESULTS

Before sildenafil therapy, no significant differences were seen between the non-nerve-sparing or nerve-sparing groups in age, interval between radical prostatectomy and start of sildenafil, presurgical and predrug erectile status, nocturnal erections, and the ability to penetrate (Table II).

The presence of the neurovascular bundles bilaterally had a significant impact on the efficacy of sildenafil ($P < 0.001$; Table III). Of the 18 patients who had undergone a bilateral nerve-sparing procedure, 12 (67%, 95% CI 41% to 87%) had a positive response, defined as an erection sufficient for penetration. Three of the 18 had undergone a unilateral nerve-sparing procedure, and none of them responded to sildenafil. Thus, the percentage of patients with bilateral nerve-sparing surgery who had a positive response was 80% (12 of 15, 95% CI 52% to 96%, $P < 0.001$; Table III).

The quality of the erection with sildenafil was excellent, as shown by the mean duration of vaginal intercourse, which was 6.92 minutes. Interestingly, the effect of sildenafil on the ability to achieve vaginal intercourse, as well as the quality of the erection, correlated with the high spousal satisfaction rate of 80%. The maximum number of doses required to achieve a positive response was

TABLE III. Comparison between patients with nerve-sparing and non-nerve-sparing prostatectomies in response to sildenafil

Patient Characteristic	Nerve-Sparing		Non-Nerve-Sparing (n = 10)	P Value*
	Bilateral (n = 15)	Unilateral (n = 3)		
No. of doses taken	4.9 ± 0.5	4.0 ± 0.0	4.7 ± 0.9	0.86
Adequate foreplay (% , n)	100 (15/15)	100 (3/3)	100 (10/10)	1.00
Able to penetrate (% , n)	80 (12/15)	0 (0/3)	0 (0/10)	<0.001
Estimated duration of intercourse (min)	6.92 ± 2.32	0 (0/3)	0 (0/10)	<0.001
Spouse satisfaction (% , n)	80 (12/15)	0 (0/3)	0 (0/10)	<0.001

* Comparison of nerve-sparing and non-nerve-sparing patient groups; P <0.05 was considered as significant.

TABLE IV. Side effects and discontinuation of sildenafil

Side Effects	Frequency (n = 28)	95% CI
Headache	11/28 (39)	22%–59%
Abnormal color vision	3/28 (11)	2%–28%
Flushing	2/28 (7)	1%–24%
Dyspepsia	1/28 (4)	0%–18%
Discontinuation	3/28 (11)	2%–28%

KEY: CI = confidence interval.
Numbers in parentheses are percentages.

patients describing a positive response with the first or second dose (Table III).

Sildenafil had no effect in the non-nerve-sparing group of 10 patients (0%, 95% CI 0% to 31%). Despite adequate foreplay and multiple doses, none of these patients reported any improvement in their erectile status.

About 39% of the patients experienced transitory headaches. The other common side effect was abnormal color vision, experienced by 11% of patients. No patients discontinued sildenafil because of side effects. Overall, the 3 patients (11%, 95% CI 2% to 28%) who did discontinue sildenafil believed the drug was ineffective (Table IV). The remaining patients who did not respond to sildenafil continued to use it in hopes of a future response.

COMMENT

The release of sildenafil has created a tremendous market for the treatment of erectile dysfunction. A recent report described a dose-response/escalation study using sildenafil in men with erectile dysfunction from various causes, but they did not specify the effect of sildenafil in the post-radical prostatectomy group.¹ Our study investigated the use of sildenafil in this patient group, and determined whether the presence or absence of the neurovascular bundles affected the response.

The most salient finding of this study is how well patients who underwent a bilateral nerve-sparing

doses, most of these patients (80%) achieved erections sufficient for vaginal intercourse. This response was directly related to spousal satisfaction, again confirming the quality of the erection. Conversely, no patient who underwent a non-nerve-sparing procedure responded. The lack of a response to sildenafil in the 3 patients who underwent a unilateral nerve-sparing procedure is unclear because of the small sample size. More patients will have to be studied in this subgroup to accurately determine the efficacy of sildenafil. However, in a unilateral nerve-sparing procedure, there may be insufficient functioning nerve tissue for the optimal release of nitric oxide and subsequent conversion of guanosine triphosphate to cyclic guanosine monophosphate.

The mean time interval from radical prostatectomy to the initiation of sildenafil was roughly 1 year in both the nerve-sparing and non-nerve-sparing groups. It is quite possible that earlier initiation of sildenafil might increase the positive response rate in both groups. Prospective studies have already been started to assess the efficacy of sildenafil at an earlier interval after radical prostatectomy.

This study has important implications in the surgical management of prostate cancer at a time when the morbidity of radical prostatectomy is being severely scrutinized. Although potency rates of 50% to 70% after nerve-sparing radical prostatectomy have been reported,^{2,3} these figures are not universally accepted. Jonler and associates,⁴ from the University of Wisconsin, report that only 9% of their patients had full erections and 38% had partial erections after nerve-sparing prostatectomy. Similar figures were reported by Fowler *et al.*⁵ in 1993 in a Medicare population. In another report, Talcott *et al.*⁶ described inadequate erections and vaginal penetration in 79% of men who underwent a bilateral nerve-sparing procedure and found no benefit after the unilateral nerve-sparing procedure. Sildenafil offers a chance to salvage roughly 80% of our impotent patients if a bilateral nerve-sparing procedure is done.

Our findings helped us reexamine the role for

inexperienced surgeon, when performing a nerve-sparing procedure, will have greater blood loss, more iatrogenic positive margins, and require more operative time. These findings should encourage urologists to continue to perform and perfect the nerve-sparing approach to give their patients the best chance of successful treatment for impotence after prostatectomy.

CONCLUSIONS

Patients with erectile dysfunction after prostatectomy responded well to sildenafil if both neurovascular bundles were spared during surgery. After a minimum trial of four doses of sildenafil, 80% of the patients who had undergone a bilateral nerve-sparing procedure could sustain erections sufficient for vaginal penetration with a mean duration of nearly 7 minutes. This positive response resulted in an 80% spousal satisfaction rate. Men in the non-nerve-sparing group showed no response to sildenafil nor did the patients who had undergone a unilateral nerve-sparing procedure. However, the unilateral nerve-sparing group was too small to draw any firm conclusions. The main side

effects of sildenafil were headaches and abnormal color vision, but none of the patients discontinued the medication because of side effects. This study has important implications concerning the benefit of a nerve-sparing radical prostatectomy.

ACKNOWLEDGMENT. To Robin Verdi for secretarial assistance.

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