Spinal Cord (2000) 38, 363–370

www.nature.com/sc

Quality of life in patients with spinal cord injury receiving VIAGRA® (sildenafil citrate) for the treatment of erectile dysfunction

C Hultling*[,1], F Giuliano[2], F Quirk[3], B Peña[4], A Mishra[4] and MD Smith[3]

[1]Spinalis SCI Research Unit, Karolinska sjukhuset Norrbacka, SE-171 76 Stockholm, Sweden; [2]Department of Urology, CHU de Bicêtre, AP-HP, Le Kremlin Bicêtre 94270 France; [3]Pfizer Ltd., Ramsgate Road, Sandwich, Kent CT13 9NJ, UK; [4]Pfizer Inc., International Pharmaceuticals Group, 235 E. 42nd Street, Mail Stop 13, New York, NY 10017, USA

Study design: A multicenter, randomized, double-blind, placebo-controlled, flexible-dose, two-way crossover study conducted June 1996 through January 1997.
Objectives: To evaluate the effect of sildenafil citrate (VIAGRA®) on the quality of life (QoL) of men with erectile dysfunction (ED) caused by spinal cord injury (SCI).
Setting: Study centers in Australia, Belgium, France, Germany, Norway, Sweden and the United Kingdom.
Methods: Questions 13 and 14 of the 15-item International Index of Erectile Function (IIEF) addressed QoL issues directly related to ED in 178 men with SCI. A 5-item questionnaire addressing concerns that men had about their erection problems was also used to evaluate the impact of ED on QoL. Several commonly used psychometric instruments, including the Medical Outcomes Survey (MOS) Short Form-12, Psychological General Well-Being Index, and MOS Family Survey, assessed general QoL issues.
Results: Significant improvements were seen for overall satisfaction with sex life (IIEF Q13), sexual relationship with partner (IIEF Q14), and concerns about erectile problems ($P<0.0001$). Improvements were reported in scores for the generic QoL parameters of mental health, well-being, depression, and anxiety ($P<0.05$ sildenafil *versus* placebo).
Conclusion: Treatment with sildenafil can significantly improve key QoL parameters in men with ED caused by SCI.
Sponsorship: This study was funded by Pfizer Inc.
Spinal Cord (2000) **38,** 363–370

Keywords: erectile dysfunction; spinal cord injury; VIAGRA®; quality of life

Introduction

Erectile dysfunction (ED) is the persistent inability to achieve and/or maintain an erection sufficient for satisfactory sexual intercourse,[1] and is a common result of spinal cord injury (SCI).[2] Although many patients with SCI retain some reflexogenic or psychogenic erectile function, these erections are frequently unsuitable for satisfactory sexual activity.[2] Treatment for ED includes injections of vasoactive substances, vacuum constrictive devices, and penile prosthesis implants.[3–7] However, these methods are cumbersome, resulting in a high rate of drop-out.[1]

VIAGRA® (sildenafil citrate) is an oral agent for the treatment of ED. Sildenafil has proven both effective and well tolerated in patients with ED of broad-spectrum etiology[8–10] and in patients with SCI.[11–13] Sildenafil selectively inhibits the enzyme phosphodiesterase (PDE) type 5, the enzyme responsible for breakdown of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum.[14,15] Sildenafil enhances the relaxant effect of nitric oxide,[15,16] which results in activation of guanylate cyclase, thereby elevating the levels of cGMP. The increased levels of cGMP lead to smooth muscle relaxation, resulting in an erection.

The National Institutes of Health (NIH) Consensus Development Panel on Impotence[1] has recommended that studies be conducted to determine the social and psychological effects of ED on patients and partners. The withdrawal of men from their intimate relationships because of fears of inadequate sexual performance or rejection may have a negative effect on overall health.[1] The evaluation and treatment of ED should be dictated by patient motivation, expectations, and physical and mental health.[17] Not only will the treatment of ED improve the male's intimate relation-

*Correspondence: C Hultling, Spinalis SCI Research Unit, Karolinska sjukhuset Norrbacka, SE-171 76 Stockholm, Sweden

ships but will also improve that of the partner, who may also experience increased anxiety[1] and a poorer quality of life (QoL).[18]

In general, average QoL scores are significantly lower in patients with SCI than in the nondisabled population.[19,20] Patients with SCI have a greater propensity for a poorer QoL than patients without SCI, not only because the injury results in physical limitations, but also because of psychosocial problems, such as barriers to social relationships and the fact that persons tend to reject close and intimate relationships with disabled people.[21] Therefore, SCI may have a profound effect on the patient's sexuality,[22] resulting in a significant decrease in satisfaction with sexual life, an important predicator of satisfaction with life as a whole.[23] Presumably, a lower QoL, primarily from the anxiety and depression that patients with SCI suffer, is exacerbated by the sense of depression and poor self-image associated with ED.[1,19,24] The trauma of the injury may also place a great strain on the sexuality of the partner in an existing relationship[25] and increase the anxiety levels of the patient with SCI. Approximately half of preinjury partners and a quarter of postinjury partners reported decreased sexual interest due to the injury.[26]

The interrelated nature of ED, SCI, and QoL warrants the inclusion in clinical trials of an assessment of QoL. This can properly address the efficacy of any therapy on overall sexual functioning and its physical, psychological, and social impact. The importance of QoL in assessing treatment in patients with SCI is underscored by the belief that levels of social and psychological functioning are more important predictors of life satisfaction than the seriousness of the injury in patients with SCI.[27]

Objectives

The efficacy of oral sildenafil to improve erections has been demonstrated in men with ED attributable to SCI;[12,13] however, any improvement in QoL resulting from improvements in sexual functioning have not yet been examined in men receiving sildenafil for the treatment of ED attributable to SCI. The efficacy of sildenafil has been assessed in the men with ED and SCI used in this investigation.[11] The evaluation of the effect of sildenafil treatment on condition-specific and general QoL parameters in men with ED caused by SCI is reported.

Methods

Study population

Quality of life (QoL) was evaluated in a randomized, double-blind, placebo-controlled, two-way crossover, flexible-dose study of 178 men with ED caused by SCI (151 men had residual psychogenic or reflexogenic erectile function and 27 men had no residual erectile function) at 19 centers in Europe and Australia. All participants conformed to specific inclusion and exclusion criteria. Main inclusion criteria were as follows: men at least 18 years of age, a traumatic SCI at least 6 months before screening, a clinical diagnosis of ED solely attributable to injury of the spinal cord, cessation of other therapies for ED, and involvement in a stable relationship with a female partner for at least the past 6 months. The main exclusion criteria were the following: laboratory abnormalities; genital anatomical deformities; primary sexual disorder other than ED; major psychiatric or psychological disorder, including major depression; diabetes mellitus; history of stroke or myocardial infarction within the last 6 months; any significant cardiovascular disease within the last 6 months; regular nitrate therapy; active peptic ulcers; history of retinitis pigmentosa, bleeding disorders, or renal or hepatic abnormalities; and evidence of other medical conditions impairing ability to complete the study. These men were the same participants used to assess the efficacy of sildenafil in patients with SCI.[11]

Patients attended the clinic on five occasions: at screening, at the start and end of the first double-blind treatment period, and at the start and end of the second double-blind treatment period. Laboratory safety tests were performed at screening and at the end of each treatment period.

Dosing

Following a 4-week run-in period, each patient underwent two 6-week crossover periods with a 2-week washout period between the crossover periods. The run-in period could be reduced to 2 weeks if patients had not taken any other treatment for their ED during the 2 weeks before screening. Patients were randomized to receive either 6 weeks of flexible-dose sildenafil treatment followed by 6 weeks of matching placebo or 6 weeks of placebo followed by 6 weeks of flexible-dose sildenafil treatment.

Patients were instructed to take 50 mg of sildenafil or matching placebo approximately 1 h before sexual activity but not more than once daily. Depending on efficacy and tolerability, the dose was increased to a maximum of 100 mg or adjusted downward to 25 mg over the 6-week treatment period. Patients were asked to complete an event log about sexual intercourse each time they took a dose of drug or engaged in sexual activity and what dosage was taken. Patients were discontinued from the study if a dose caused unacceptable adverse events.

Clinical assessments

The efficacy of sildenafil treatment on the improvement on erections was evaluated using a global efficacy question ('Did treatment improve your erections?'). The validated 15-item International Index of Erectile Function (IIEF) is a reliable, self-administered questionnaire with the sensitivity and specificity for detecting treatment-related changes in patients with ED in

research or clinical settings.[28] The 15 questions of the IIEF can be divided into five domains that address erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction with sexual life. Patients completed the IIEF at baseline and at the end of treatment for each treatment period.

Responses to questions 13 and 14 of the IIEF, which comprise the overall satisfaction with sexual life domain of the IIEF, specifically address QoL issues related to sexual dysfunction. Question 13 asks, 'How satisfied have you been with your overall sex life? and question 14 asks, 'How satisfied have you been with your sexual relationship with your partner?' These questions are scored on a scale of 1 ('very dissatisfied') to 5 ('very satisfied'). Responses to other IIEF questions were previously published.[11]

Quality of life was also assessed using one instrument specifically designed to assess the impact of erectile problems on QoL and four broad-based, psychometric QoL instruments that are commonly used for comparisons involving generic health concepts at baseline and at the end of each 6-week treatment period (Table 1). The specific impact of erectile problems on QoL was assessed using the 5-item Impact of Erectile Problems questionnaire.[29] The five questions ask about concerns associated with erection problems (feelings of frustration, discouragement, despair, worry, and being weighed down by erectile problems). Each question is scored on a scale of 1 ('all of the time') to 6 ('none of the time').

The general QoL instruments, which address more global concepts of life satisfaction (see Table 1 for scoring scales and types of questions), included the 12-item Medical Outcomes Survey Short Form (MOS SF-12),[30] adapted from the 36-item MOS SF-36 survey,[31] and the 14-item Psychological General Well-Being (PGWB) Index, adapted from the 22-item PGWB Index.[32] The MOS SF-12 is a brief measure of overall functional health (mental and physical) status,[33] and the PGWB Index is a measure of psychological well-being.[32] Questions 3 and 4 from the SF-12 questionnaire were not applicable to patients with SCI and therefore not completed. Individual scores for survey questions in these two instruments were summed by physical and mental health components for the MOS SF-12 survey and by anxiety, positive well-being, self-control, and

Table 1 Quality-of-life instruments for generic health concepts

Quality-of-life endpoint	*Construct*	*Item content (Number of items)*
MOS* Short Form 12: Mental health	Summary score of perceived social and emotional functioning	Energy, emotional problems affecting work or daily activities, interference with social activities, feeling low/down-hearted (6)
MOS* Short Form 12: Physical health	Summary score of perceived physical function and general health	Ability to perform moderate activities, perceived general health, pain, limited in work/daily activities (6)
MOS* health compared to 1 year ago (baseline) (MOS SF-36 question 2)	Perceived general health relative to 1 year ago	'Compared to 1 year ago, how would you rate your health in general now?' (1)
PGWB: Anxiety†	Generalized anxiety	Bothered by nervousness; generally tense, worried or upset, relaxed at ease, or agitated and wound up; under strain or stress (5)
PGWB: Positive Well-being†	General well-being	General spirits, satisfied with personal life, interesting daily life, cheerful and light-hearted (4)
PGWB: Self-control†	Emotional stability and in control	Control of behavior, thoughts and emotions; losing control over way to act, talk, think, or feel; emotionally stable and sure of self (3)
PGWB: Depression†	General depression	Feeling depressed, feeling discouraged and hopeless (2)
MOS* Family Survey (Q1 – Q6)	Intrapersonal communication with partner	Say anything wanted to say, trouble sharing personal feelings, difficulty airing feelings, feeling close to partner, partner supportive, rely on other people (6)
MOS* Family Survey: Satisfaction with Relationship (Q7)	Relationship with partner satisfaction	How happy, pleased, satisfied with your relationship with partner (1)
Impact of Erectile Problems	Emotional distress related to erectile problems	Feelings of frustration, discouragement, despair, worry, and being weighed down by erectile problems (5)

*MOS = Medical Outcomes Study. †Components of the Psychological General Well-Being (PGWB) Index of mental well-being

depression components for the PGWB survey. The other general QoL instrument was 7-item MOS Family Survey (evaluated by composite scores for six questions related to interpersonal communications in general and scores for a seventh question specifically addressing partner relationship).[34] A single question from the MOS SF-36 survey was used to compare overall current health status to health status 1 year ago.

Statistical analysis

Patients with residual (psychogenic and/or reflexogenic) erectile function and patients with no residual erectile function at baseline were included in all analyses, unless noted differently. Responses to IIEF questions, the partner questionnaire, and QoL data were analyzed using analysis of covariance (ANCOVA) and included terms for treatment effect, center effect, baseline effect, treatment-by-baseline interaction, and treatment-by-center interaction. Age, duration of ED, smoking status, period, sequence (carryover), and residual erectile function status were used as covariate terms. Results using ANCOVA for these data have been successfully submitted in regulatory filings for sildenafil. Efficacy and QoL comparisons were made between sildenafil (all doses) and placebo. All tests were two-tailed and evaluated at the 5% level for significance of treatment effect (that is, sildenafil *versus* placebo).

Safety analysis

Adverse events that occurred during treatment or within 7 days of the end of treatment were recorded and are as previously reported.[11] The level of discontinuation during sildenafil treatment (3.4%) was similar to that during placebo treatment (2.3%).

Results

The demographics of the 178 patients randomized to treatment in the two sequence groups were nearly identical and are shown in Table 2. The mean age of patients with SCI in both sequence groups was 38 years (range 19–63 years) with 11 years mean duration of SCI since its diagnosis for both sequence groups. Approximately 85% of the patients reported residual erectile function at baseline; 15% reported no residual erectile function at baseline. Patients in both sequence groups also showed a similar tendency in dosage of sildenafil and placebo taken (Table 3). There was a trend toward taking the higher doses of placebo (ranging from 4% at 25 mg to 81% at 100 mg) than of sildenafil (5% at 25 mg to 59% at 100 mg).

Because sexual function affects QoL, it was necessary to assess that oral sildenafil improved sexual function in the patients with SCI in this study. Published results on the same study population found a significantly improved ability to have intercourse for patients with SCI who received sildenafil (80%) compared with those who received placebo (10%), a significant preference for sildenafil treatment over placebo by 95% of the patients, and statistically significant improvements in the ability to obtain and maintain erections with sildenafil treatment *versus* placebo ($P<0.0001$).[11] Patients (64%) with no residual erectile function also stated a preference for sildenafil *versus* placebo.[11]

Queries from the IIEF relating treatment to overall satisfaction with sex life (Q13) and sexual relationship with partner (Q14) resulted in significant improvements with sildenafil treatment compared with placebo ($P<0.0001$) (Figure 1). The mean score for Q13 of the IIEF increased by 49% over baseline for patients receiving sildenafil, which was significantly greater

Table 2 Demographics

	Sildenafil→Placebo	*Placebo→Sildenafil*
Number of patients	89	89
Age range (years)	19–63	18–63
Mean age (years)	38	38
Mean duration of SCI (years)	11.7	10.3
Range of SCI since first diagnosis (years)	0.74–38	0.70–35

SCI = spinal cord injury

Table 3 Dosage and frequency of treatment drug

Dosage	*Sildenafil*			*Placebo*		
	25 mg	*50 mg*	*100 mg*	*25 mg*	*50 mg*	*100 mg*
Treatment sequence (6 weeks Sildenafil → 6 weeks Placebo)						
Baseline	–	89	–	–	85	–
End of treatment	4	34	51	3	15	67
Treatment sequence (6 weeks Placebo → 6 weeks Sildenafil)						
Baseline	–	86	–	–	89	–
End of treatment	4	30	51	4	13	72

than the 1% decrease from baseline in mean score for patients receiving placebo. The mean score for Q14 of the IIEF increased by 34% above baseline for patients receiving sildenafil. For Q14, patients receiving placebo showed no significant change (2%) from overall baseline mean score. Improvements in scores in men receiving sildenafil for questions concerning QoL and sexual function were mirrored by decreased concerns about erectile problems. The 'impact of erectile problems' parameter directly assessed emotional distress related to ED. Scores for the 5-item Erectile Problems questionnaire improved by almost 23% above baseline values in men receiving sildenafil compared with only a 4% improvement in scores for men receiving placebo ($P<0.0001$ for treatment effect) (Table 4; Figure 2).

Statistically significant ($P<0.05$) improvements in favor of sildenafil at the end of treatment were seen in four out of the 10 general mental, physical, and psychosocial parameters. These improvements are shown in Table 4 and were the PGWB Index parameters of 'anxiety', 'depression', and 'well-being' and the MOS SF-12 mental health component summary score. At the end of treatment, the mean score for PGWB 'depression' decreased with placebo

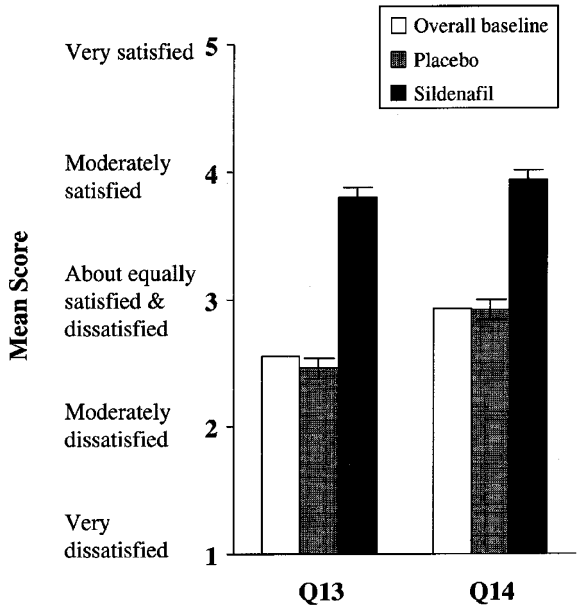

Figure 1 Effect of treatment on overall satisfaction with sex life and sexual relationship with partner. Patient responses to question 13 (overall satisfaction with sex life) and question 14 (overall satisfaction with sexual relationship with partner) of the IIEF were recorded at baseline and the end of treatment. The per cent changes from baseline to end of treatment for patients receiving sildenafil and placebo are shown. Scores ranged from 1 ('very dissatisfied') to 5 ('very satisfied'). SEM bars are included. $P<0.0001$ sildenafil *versus* placebo

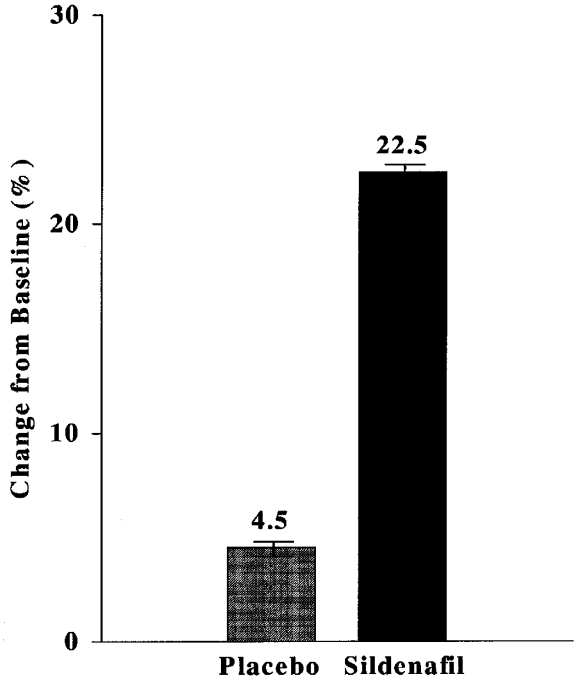

Figure 2 Effect of treatment on total scores for the 5-item Impact of Erectile Problems questionnaire. The summary score improved significantly with sildenafil treatment *versus* placebo. The per cent changes from baseline to end of treatment for patients receiving sildenafil and placebo are shown. SEM bars are included. $P<0.0001$ sildenafil *versus* placebo

Table 4 Effect of treatment on QoL*

QoL parameter	*No. of questions*	*Score range*	*Overall baseline*	*End-of-treatment*		P *value*	*95% CI*
				Placebo	*Sildenafil*	*S* vs *P*	*S–P*
Impact of erectile problems	5	5–30	20.0	20.9	24.5	<0.0001	2.77–4.50
SF-12 Mental health	5	0–100	49.4	50.1	51.3	0.012	0.28–2.26
Depression	4	0–10	8.9	8.8	9.0	0.014	0.04–0.44
Positive well-being	2	0–20	12.4	13.0	13.4	0.041	0.02–0.82
Anxiety (all)	5	0–25	19.6	19.8	20.3	0.043	0.01–0.93
Anxiety (residual)	5	0–25	19.4	19.8	20.2	0.145	−0.14–0.91

*The mean raw score at baseline and end of treatment, score range, and the number of questions per parameter are listed. Anxiety scores are listed for all patients with SCI and patients with SCI with residual erectile function at baseline. P = placebo; QoL = quality of life; S = Sildenafil; SF = short form

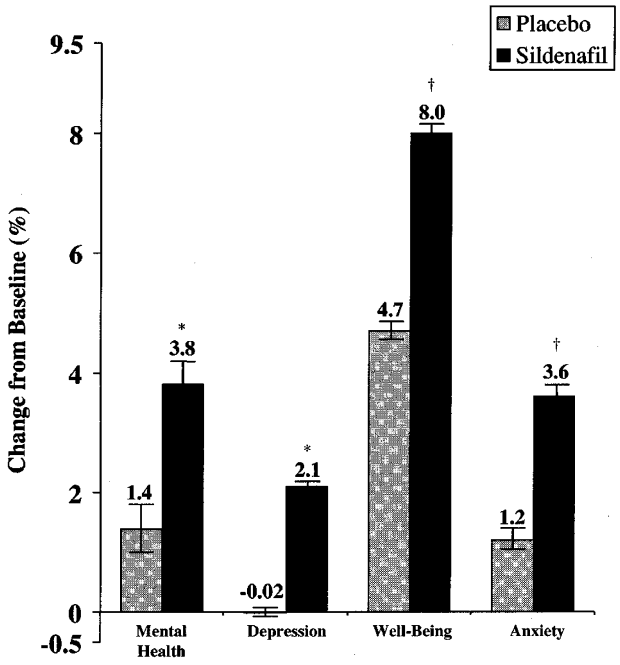

Figure 3 Effect of treatment on general concept QoL parameters. Per cent changes from baseline to end of treatment are shown for SF-12 Mental Health, PGWB Depression, PGWB Well Being, and PGWB Anxiety. SEM bars are included. *$P=0.01$; †$P=0.04$ for sildenafil *versus* placebo

and improved with sildenafil ($P=0.01$ for treatment effect) (Figure 3). Although the difference is statistically significant, it may not be clinically significant. The mean scores for the other three parameters improved by 3.6% to 8% from baseline for patients receiving sildenafil *versus* 1.2% to 4.7% for patients receiving placebo ($P<0.05$ for treatment effect for all comparisons) (Figure 3).

There were no significant differences in end-of-treatment scores between patients receiving sildenafil and patients receiving placebo for the PGWB Index measure of self-control, the MOS Family Survey, health compared with 1 year ago, or the MOS SF-12 physical summary score.

Discussion

Seventy-eight per cent of SCI lesions are in persons 40 years of age or younger.[35] Although SCI profoundly affects the patient's sexuality[22] at any age, some older men with SCI may be willing to accept ED more than younger patients with SCI.[36] An increasingly younger patient population with SCI and greatly improved survival rates in patients with SCI have shifted the treatment emphasis toward enhancing the quality of life.[2] Because sexuality is an important factor in QoL[23] and ED is a common consequence of SCI, assessing QoL in patients with SCI is an important part of treatment as well as a way of assessing the overall efficacy of therapeutic interventions for ED. A previous report indicated an improvement in QoL with a vacuum erection device but a loss of erection during sexual activity, resulting in 67% discontinuation of treatment in the sample population.[36] Penile prostheses and prostaglandin E_1 treatment improved the QoL of patients with SCI as well; however, for patients with SCI and ED, complications resulted from penile implants and prostaglandin E_1 treatment,[6,36,37] underscoring the importance of an effective and noninvasive treatment for ED.

To determine if sildenafil was effective in improving QoL in patients with SCI and ED, the effects of sildenafil on ED in patients with SCI for improvement of sexual function were examined, and those results have been published.[11] Almost all patients with SCI who reported significant improvement in the ability to have intercourse with sildenafil treatment would continue sildenafil treatment if it were available. Improvement in the ability to have intercourse was reflected in the responses to IIEF questions concerning frequency of penetration and frequency of maintained erections. These results are similar to those reported for nondisabled men with ED.[8] Oral sildenafil has previously been found to be effective in improving sexual function in men with SCI.[12,13]

Because sexual dysfunction, SCI and QoL are interrelated and treatment with oral sildenafil has been found to be effective in improving sexual function, it was expected that sildenafil would improve QoL in patients with SCI and ED. All parameters specifically relating QoL and ED showed significant improvements in the mean scores. Patients with SCI reported increased satisfaction with their sex life (Q13 of the IIEF) and their sexual relationship (Q14 of the IIEF). Patients also were less concerned about their erectile problems (for example, less worry, frustration, despair) than patients receiving placebo. A previous study found that patients with SCI taking sildenafil did report an improvement in satisfaction with their sex life, but this study was limited by the small number of patients (12), limited number of QoL assessments, and inclusion only of men with SCI with reflexogenic erections.[13]

The lack of improvement in mean scores in response to the general satisfaction with relationship question (MOS Q7) in this study may be due to the criteria for patients in this study, which included patients with SCI who were in a stable relationship and had a traumatic SCI 6 months before screening. A sexual relationship for patients with SCI is unlikely to be spontaneous: patients and their partners are more likely to have discussed sex in advance, allowing for patients with SCI to have overcome or learned to deal with their ED. Patients with SCI in postinjury marriages were significantly more satisfied than patients with SCI in preinjury marriages with their living arrangements and sex lives ($P<0.001$), as well as their social lives, general health ($P<0.01$), emotional adjustment, and sense of control over their lives

($P<0.05$).[38] Litwin and colleagues[39] showed that there was no significant correlation between sexual bother (level of interference or annoyance by ED) and marital interaction in men with ED, and sexual bother did not correlate with any of the general QoL domains.

Other QoL instruments used in this study did not specifically relate sexual function with QoL, yet there were statistically significant improvements following treatment with sildenafil in four of the QoL parameters. There were statistically significant ($P<0.05$) improvements in the MOS SF-12 mental health component (psychological distress and well-being) score and the PGWB positive well-being, depression, and anxiety indices. An improvement in mental health and positive well-being is likely due to an improved sex life, improved sexual relationship with partner, and reduced concerns about erectile problems and inadequate sexual performance. A high association between overall well-being and emotional problems and sexual dysfunction was recently reported.[40]

It is important to note that there were significant improvements in mean scores of anxiety and depression with sildenafil treatment. Both anxiety and depression are primary psychological consequences of SCI.[24] Anxiety and depression significantly improved with sildenafil, suggesting that decreased sexual functioning does diminish QoL in patients with SCI, despite other reports. A significant improvement in anxiety was not seen in patients with residual erectile function. This suggests that improvement in erectile function reduced anxiety most in patients with no residual erectile function at baseline. There was a decline in the depression index with placebo treatment, indicating an increased level of depression at the end of the treatment compared to baseline. It is possible that the expectation of success led to discouragement and a decline in the placebo-treated patients. Patients were excluded from this study if they had depression, and this sample population is not representative of the total SCI male population. The exclusion of patients with depression will give higher overall baseline values than would normally be seen in a group of men without such an exclusion criterion.

A shortcoming of this study may be that results were based on only 6 weeks of treatment with sildenafil, and it is possible that with a larger sample size and a longer duration of sildenafil treatment, significant changes in other QoL parameters would be seen. Studies measuring effectiveness of other ED therapies on QoL in nondisabled men did not show significant improvements until 6 months after baseline.[18,41]

Not all QoL parameters measured in this study showed statistically significant improvements because an improvement in erectile function is unlikely to improve perceived general health, physical function, emotional stability, and general communication and satisfaction with partner. This may be explained by the relatively high baseline scores, due to the strict inclusion criteria, allowing little room for improvement. Patients with SCI in a relationship are more likely to have adapted other means of sexual gratification, especially among younger couples.[26] The same study reported that many relationships were satisfactory in which one person has an SCI, even in the absence of sexual activity.[26] Although patients with SCI may be able to cope with their lack of sexual performance by either avoidance (38% of male patients with SCI never try sexual intercourse after their injury[42]) or other means, this does not suggest that men with ED attributable to SCI cannot improve their QoL and their sexual functioning through treatment with sildenafil.

This report finds that the QoL of men with ED attributable to SCI is significantly improved with oral sildenafil treatment. QoL parameters directly related to sexual function showed the greatest improvement. Some general QoL parameters also showed significant improvements and are the parameters most likely affected by a patient with SCI and ED. Other QoL parameters were perhaps not sensitive enough to detect important changes in patients with SCI with ED. These results demonstrate the importance of using condition-specific parameters to address the interrelatedness of QoL, SCI, and ED.

Conclusions

Treatment with sildenafil can significantly improve erectile function in men with SCI, including men with no residual erectile function.[11] Overall, the condition-specific QoL measures related to sexual function showed significant improvements after treatment with sildenafil and correlated well with the efficacy in men with ED attributable to SCI. The most dramatic improvement in QoL was seen in the overall satisfaction with sexual life domain of the IIEF, followed by being less bothered by the 'impact of erectile problems' and improvements in 'mental health' and 'depression'. No significant improvements were seen in perceived general health, physical function, emotional stability, and general communication and satisfaction with partner.

References

1 NIH Consensus Development Panel on Impotence. Impotence. *JAMA* 1993; **270:** 83–90.
2 Smith EM, Bodner DR. Sexual dysfunction after spinal cord injury. *Urol Clin North Am* 1993; **20:** 535–542.
3 Bodner DR *et al*. The application of intracavernous injection of vasoactive medications for erection in men with spinal cord injury. *J Urol* 1987; **138:** 310–311.
4 Bodner DR, Leffler B, Frost F. The role of intracavernous injection of vasoactive medications for the restoration of erection in spinal cord injured males: a three year follow up. *Paraplegia* 1992; **30:** 118–120.
5 Collins KP, Hackler RH. Complications of penile prostheses in the spinal cord injury population. *J Urol* 1988; **140:** 984–985.

6 Kimoto Y and Iwatsubo E. Penile prostheses for the management of the neuropathic bladder and sexual dysfunction in spinal cord injury patients: long term follow up. *Paraplegia* 1994; **32:** 336–339.
7 Watanabe T *et al*. Epidemiology of current treatment for sexual dysfunction in spinal cord injured men in the USA model spinal cord injury centers. *J Spinal Cord Med* 1996; **19:** 186–189.
8 Goldstein I *et al*. Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* 1998; **338:** 1397–1404.
9 Morales A *et al*. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998; **10:** 69–74.
10 Padma-Nathan H *et al*. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction: a double-blind, placebo-controlled study of 329 patients. *Int J Clin Pract* 1998; **52:** 375–380.
11 Giuliano F *et al*. Randomized trial of sildenafil for the treatment of erectile dysfunction in spinal cord injury. *Ann Neurol* 1999; **46:** 15–21.
12 Maytom MC *et al*. A two-part pilot study of sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Spinal Cord* 1999; **37:** 110–116.
13 Derry FA *et al*. Efficacy and safety of oral sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Neurology* 1998; **51:** 1629–1633.
14 Rajfer J *et al*. Nitric oxide as a mediator of relaxation of the corpus cavernosum in response to noradrenergic, noncholinergic neurotransmission. *N Engl J Med* 1992; **326:** 90–94.
15 Boolell M *et al*. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. *Int J Impot Res* 1996; **8:** 47–52.
16 Ballard SA *et al*. Sildenafil, an inhibitor of phosphodiesterase type 5, enhances nitric oxide mediated relaxation of human corpus cavernosum [Abstract]. *Int J Impot Res* 1996; **8:** 103.
17 Carrier S, Zvara P, Lue TF. Erectile dysfunction. *Endocrinol Metab Clin North Am* 1994; **23:** 773–782.
18 Gheorghiu S *et al*. Quality of life in patients using self-administered intracavernous injections of prostaglandin E1 for erectile dysfunction. *J Urol* 1996; **156:** 80–81.
19 Kannisto M, Sintonen H. Later health-related quality of life in adults who have sustained spinal cord injury in childhood. *Spinal Cord* 1997; **35:** 747–751.
20 Dijkers M. Quality of life after spinal cord injury: a meta analysis of the effects of disablement components. *Spinal Cord* 1997; **35:** 829–840.
21 Scivoletto G, Petrelli A, Di Lucente L, Castellano V. Psychological investigation of spinal cord injury patients. *Spinal Cord* 1997; **35:** 516–520.
22 Goddard LR. Sexuality and spinal cord injury. *J Neurosci Nurs* 1988; **20:** 240–244.
23 Fugl-Meyer AR *et al*. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997; **9:** 141–148.
24 Scivoletto G *et al*. Psychological investigation of spinal cord injury patients. *Spinal Cord* 1997; **35:** 516–520.
25 Kreuter M *et al*. Partner relationships, functioning, mood and global quality of life in persons with spinal cord injury and traumatic brain injury. *Spinal Cord* 1998; **36:** 252–261.
26 Kreuter M, Sullivan M, Siosteen A. Sexual adjustment after spinal cord injury–comparison of partner experiences in pre- and postinjury relationships. *Paraplegia* 1994; **32:** 759–770.
27 Post MW *et al*. Predictors of health status and life satisfaction in spinal cord injury. *Arch Phys Med Rehabil* 1998; **79:** 395–401.
28 Rosen RC *et al*. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997; **49:** 822–830.
29 Feldman HA *et al*. Construction of a surrogate variable for impotence in the Massachusetts Male Aging Study. *J Clin Epidemiol* 1994; **47:** 457–467.
30 Ware JE, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales preliminary test of reliability and validity. *Medical Care* 1996; **34:** 220–233.
31 Ware Jr, JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30:** 473–483.
32 Neugarten BL, Havighurst RJ and Tobin SS. The measurement of life satisfaction. *J Gerontol* 1961; **16:** 134–143.
33 Stewart AL, Hays RD, Ware Jr JE. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 1988; **26:** 724–735.
34 Stewart AL, Ware JE. Duke University Press: Durham 1992.
35 National Spinal Cord Injury Statistical Center. Annual Report for the Model Spinal Cord Injury Care Systems. 1994.
36 Denil J, Ohl DA, Smythe C. Vacuum erection device in spinal cord injured men: patient and partner satisfaction. *Arch Phys Med Rehabil* 1996; **77:** 750–753.
37 Vaidyanathan S, Soni BM, Krishnan KR. Special precautions to be observed while using alprostadil in patients with spinal cord injury [letter]. *Spinal Cord* 1997; **35:** 402–403.
38 Crew NM, Krause JS. Marital relationships and spinal cord injury. *Arch Phys Med Rehabil* 1988; **69:** 435–438.
39 Litwin MS, Nied RJ, Dhanani N. Health-related quality of life in men with erectile dysfunction. *J Gen Intern Med* 1998; **13:** 159–166.
40 Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA* 1999; **281:** 537–544.
41 Willke RJ *et al*. Quality of life effects of alprostadil therapy for erectile dysfunction. *J Urol* 1997; **157:** 2124–2128.
42 Levitt R. Understanding sexuality and spinal cord injury. *J Neurosurg Nurs* 1980; **12:** 88–89.