The Efficacy and Safety of Oral Sildenafil in Thai Men with Erectile Dysfunction : A Randomized, Double-Blind, Placebo Controlled, Flexible-Dose Study†

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Abstract

Objective : To evaluate the efficacy and safety of sildenafil citrate (Viagra™) in a randomized, double-blind, placebo-controlled, flexible-dose study in Thai men with erectile dysfunction of broad-spectrum etiology and more than 6 months' duration.

Material and Method : 125 patients aged 26 to 77 years were randomized at 4 centers in Thailand to receive either sildenafil citrate (50 mg initially, increased if necessary up to 100 mg or decreased to 25 mg depending on efficacy and/or tolerability) (n = 63) or a matching placebo (n = 62) taken on an 'as needed' basis approximately 1 hour prior to anticipated sexual activity for a period of 12 weeks. Efficacy was assessed by the patients' responses to the 15-question International Index of Erectile Function (IIEF), to questions on the event log of sexual activity, and to the global efficacy assessment question concerning improvement in erections.

Results : At the conclusion of the study, both the primary efficacy variables relating to the achievement and maintenance of erections sufficient for sexual intercourse and the secondary efficacy variables, which included the 5 separate domains of sexual functioning of the IIEF, the percentage of successful attempts at sexual intercourse, and the global efficacy assessment question concerning improvement in erections, were all significantly improved statistically by sildenafil in comparison with placebo except in the sexual desire domain which showed no difference. The percentage of successful attempts at sexual intercourse in the sildenafil group was 66.16 per cent while in the placebo group it was 33.05 per cent. The percentage of global efficacy assessment was improved in the sildenafil group by 82.5 per cent compared to 36.1 per cent in the placebo group. Adverse events considered treatment-related occurred in 19 patients (30.2%) receiving sildenafil and 7 (11.3%) receiving placebo. The most common adverse events with sildenafil were vasodilatation (flushing), headache, and dizziness, which occurred in 14.3 per cent, 6.3 per cent, and 6.3 per cent of patients respectively. All events were mild in nature.

Conclusions : Sildenafil is a safe and effective treatment for erectile dysfunction of broad-spectrum etiology in Thai men. Its efficacy appears similar to that reported in other studies in Western populations.

Key word : Erectile Dysfunction, Sildenafil, Efficacy, Safety

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+ Asian Sildenafil Efficacy and Safety Study, # 2
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Erectile dysfunction is a distressing disorder that has a significant negative impact on the quality of life of sufferers. Currently, a number of effective therapies are available to treat erectile dysfunction, including psychosexual counseling (for those with a significant psychogenic component), intracavernosal injections or transurethral delivery of alprostadil (prostaglandin E_1), vacuum-constriction devices, implanted penile prostheses, and arterial or venous surgical procedures[1-3]. A number of orally administered drugs have also been evaluated, including yohimbine, trazodone and phentolamine[1,4-8], but their effectiveness has either not been adequately demonstrated, or only demonstrated in small numbers of patients or certain subsets of erectile dysfunction.

Recent clinical studies have shown sildenafil, an orally active inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5[9], to be effective in improving erectile dysfunction of various etiologies[10-15]. In addition, its effectiveness has also been demonstrated in various subsets of erectile dysfunction patients, including those with diabetes mellitus[16], spinal cord injury[17], antidepressant-induced erectile dysfunction[18], and following radical prostatectomy[19]. These studies were mainly conducted in men living in Western countries and, as yet, its efficacy in Asian populations has not been fully evaluated. An epidemiologic study of 40-70 year-old Thai men by the TEDES group from November to December 1998 found that 37.5 per cent of them suffered from erectile dysfunction [20]. Having established the high incidence of ED in Thai men, the authors subsequently investigated the efficacy and safety of sildenafil in Thai men. This study was part of the ASSESS-2 (Asian Sildenafil Efficacy and Safety Study, #2) trial which was carried out in 3 countries (Hong Kong, Indonesia, and Thailand).

MATERIAL AND METHOD

Study population

The Thai arm of the ASSESS-2 study was conducted at 4 centers from July 1997 to March 1998. The study population was 125 Thai men aged 26 to 77 years who had a well-documented history (> 6 months) of erectile dysfunction (NIH definition)[21] of organic, psychogenic, or mixed etiology.

The patients were required to be in a stable heterosexual relationship for at least the previous six months and not to have any of the following conditions: erectile dysfunction caused by genital anatomical abnormalities or spinal cord injury; other coexis-

ting sexual disorders, e.g., hypoactive sexual desire; raised serum prolactin levels or a low free testosterone level; a major psychiatric disorder or a history of alcohol or substance abuse; major hematological, renal or hepatic diseases; diabetes mellitus that was poorly controlled or associated with untreated proliferative retinopahty; a history of stroke or myocardial infarction within the previous 6 months; hypotension or any other significant cardiovascular disease; or a history of retinitis pigmentosa. Patients were also excluded if they were receiving drugs known to be causally associated with erectile dysfunction, androgen therapy, trazodone, nitrates or nitric oxide donor compounds (in any form), and if they were using vacuum devices of any other treatments for erectile dysfunction. The study was conducted under ICH-GCP guidelines.

Initially, the patients underwent a 4-week run-in period during which baseline data on their sexual activities were collected, a full medical/drug history, physical examination, 12-lead ECG and standard laboratory safety tests were performed, and sitting blood pressure and heart rate were measured. They were required to undergo another five clinic visits - at the start of treatment (week 0) and thereafter at weeks 2, 4, 8 and 12.

Study medication

Following the run-in period, eligible patients were randomized to receive either sildenafil (Viagra™) or a matching placebo in a double-blind manner for a period of 12 weeks. For the first 2 weeks of the study, patients were instructed to take a 50 mg sildenafil tablet (or a matching placebo). At subsequent visits and at the discretion of the investigator, either an increase to 100 mg (if the response was not adequate) or a decrease to 25 mg (if higher doses were not well tolerated) was allowed.

Assessment of efficacy

The efficacy was assessed *via* the 15-question International Index of Erectile Function (IIEF) (22), patients' event log (diary) of sexual activity, and *via* a global efficacy question assessing improvement in erections at the end of treatment or at discontinuation. The primary efficacy variables were the patients' ability to penetrate their partners during sexual intercourse and to maintain the erection after penetration. The secondary efficacy variables were: 1) erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction 2) event log responses regarding the success of attempts at sexual intercourse; and 3) a global efficacy assessment in response to the question: "Has the treatment you have been taking over the past four weeks improved your erections?"

Assessment of safety

Patients were assessed for adverse events at each visit. Sitting blood pressure, heart rate and details of concomitant medications were also recorded at each visit, and a physical examination, 12-lead ECG and standard hematologic and blood chemistry tests were repeated at the end-of-treatment visit (week 12).

Statistical analysis

Each of the two primary efficacy variables was analyzed separately using univariate analysis of covariance (ANCOVA). All tests of hypotheses were performed at the 5 per cent significance level using two-sided tests of significance.

RESULTS

The baseline characteristics of the 125 patients who were randomized and took the study medication are shown in Table 1. The mean age and body weight of the two groups was similar, as were the mean duration of erectile dysfunction, smoking history, and the distribution of the primary diagnosis, i.e., organic, psychogenic or mixed etiology. The majority (> 88%) of the subjects had erectile dysfunction of organic etiology.

The intent-to-treat population comprised 125 patients (63 sildenafil, 62 placebo). One patient was lost to follow-up (placebo). The evaluable population therefore comprised 124 patients (63 sildenafil, 61 placebo).

The median duration of treatment was 84.0 days for the sildenafil group and 83.0 days for the placebo group. Treatment did not have to be permanently withdrawn in any patients in either group, although three patients receiving sildenafil and one receiving placebo required dose reductions due to the occurrence of adverse events.

Primary efficacy variables

The mean scores for IIEF questions 3 and 4 at baseline and at the end of treatment for the populations of the sildenafil and placebo groups are shown in Fig. 1 and Fig. 2. These two questions have a

Table 1. Baseline characteristics of the 125 patients randomized to treatment with either sildenafil or placebo.

Characteristics	Sildenafil (n = 63)	%	Placebo (n = 62)	%
Mean age, years (range)	54.4 (31-76)		56 (26-77)	
Mean body weight, kg (range)	68.4 (54-90)		68.8 (49-90)	
Smoking history				
Smokers	11	17.5	9	14.5
Ex-smokers	21	33.3	21	33.9
Never smoked	31	49.2	32	51.6
Duration of erectile dysfunction (years)				
≤ 2 years	42	66.7	35	56.5
> 2 to ≤ 5 years	15	23.8	20	32.3
> 5 years	6	9.5	7	11.3
Etiology of erectile dysfunction*				
Organic	41	65.1	39	62.9
Psychogenic	7	11.1	6	9.7
Mixed	15	23.8	17	27.4
Severity of erectile dysfunction at baseline				
Mild (EF domain 22-25)	6	9.5	6	9.7
Mild/Moderate (EF domain 17-22)	11	17.5	10	16.1
Moderate and severe (EF domain 11-16 and ≤ 10)	45	71.4	45	72.6

* Based on medical history and clinical assessment.

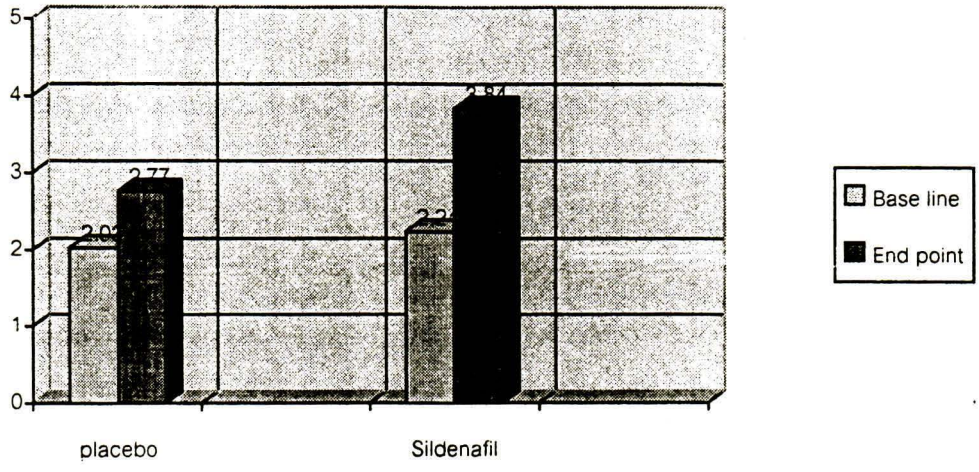

Fig. 1. Mean scores of the International Index of Erectile Function (IIEF) scores, at baseline and following 12 weeks of sildenafil or placebo administration for the primary efficacy variables: Frequency of penetration (IIEF question 3); p = 0.0001 *versus* placebo.

maximum score of 5 (almost always or always able to penetrate the partner or maintain an erection after penetration) and a minimum score of 0 (did not attempt intercourse). Sildenafil showed a highly statistically significant treatment effect with an increased frequency of penetration and erection maintenance compared with placebo (p = 0.0001).

Secondary efficacy variables

The mean scores at baseline and at the end of treatment for the five IIEF domains of sexual functioning, i.e., erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction), for the populations of the two groups are shown in Fig. 3. For all domains except sexual

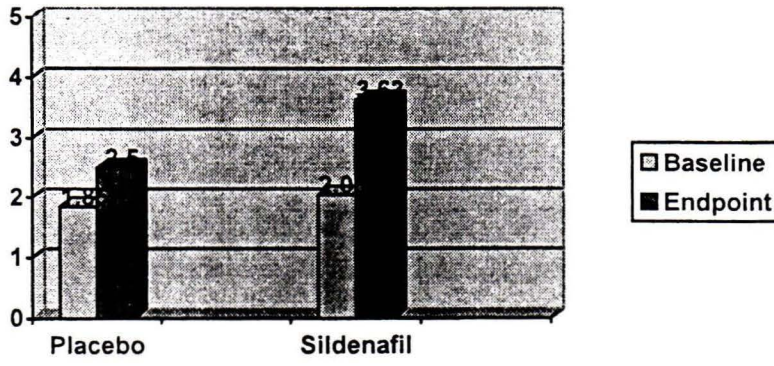

Fig. 2. Mean scores of the International Index of Erectile Function (IIEF) scores, at baseline and following 12 weeks of sildenafil or placebo administration for the primary efficacy variables: Frequency of maintained erection after penetration (IIEF question 4); p = 0.0001 *versus* placebo.

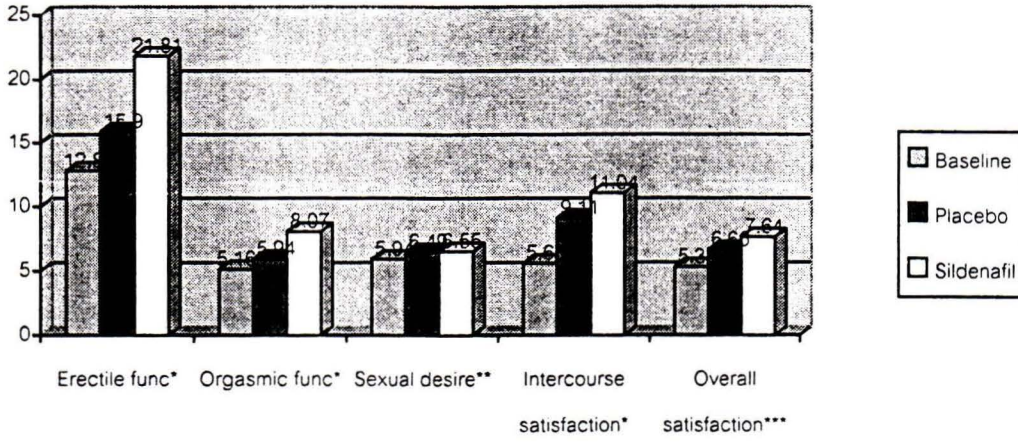

Fig. 3. Mean scores of the International Index of Erectile Function (IIEF) domain scores, at baseline and following 12 weeks of sildenafil or placebo administration for: (a) erectile function (IIEF questions 1 to 5 and 15); (b) orgasmic function (IIEF questions 9 and 10); (c) sexual desire (IIEF questions 11 and 12); (d) intercourse satisfaction (IIEF questions 6,7 and 8); and (e) overall satisfaction (IIEF questions 13 and 14). Each IIEF question has equal scores of 5. *p = 0.0001 *versus* placebo; **p = 0.7996 *versus* placebo; ***p = 0.0054

desire, sildenafil was statistically significantly more effective than placebo (p = 0.0001 or p = 0.0054). However, responses to the individual questions of the IIEF showed that for four assessments: 1) frequency of sexual intercourse (question 6), 2) frequency of sexual desire (question 11), 3) the level of sexual desire (question 12), and 4) relationship satisfaction (question14), there was no statistically significant difference between the two groups. Global efficacy assessment showed improvement of 82.5 per cent in sildenafil group compared with 36.1 per cent in the placebo group (Fig. 4).

Adverse events

All 125 patients who were randomized and took the study medication were included in the adverse event analysis. Table 2 lists the adverse events recorded during the trial, regardless of causality, classi-

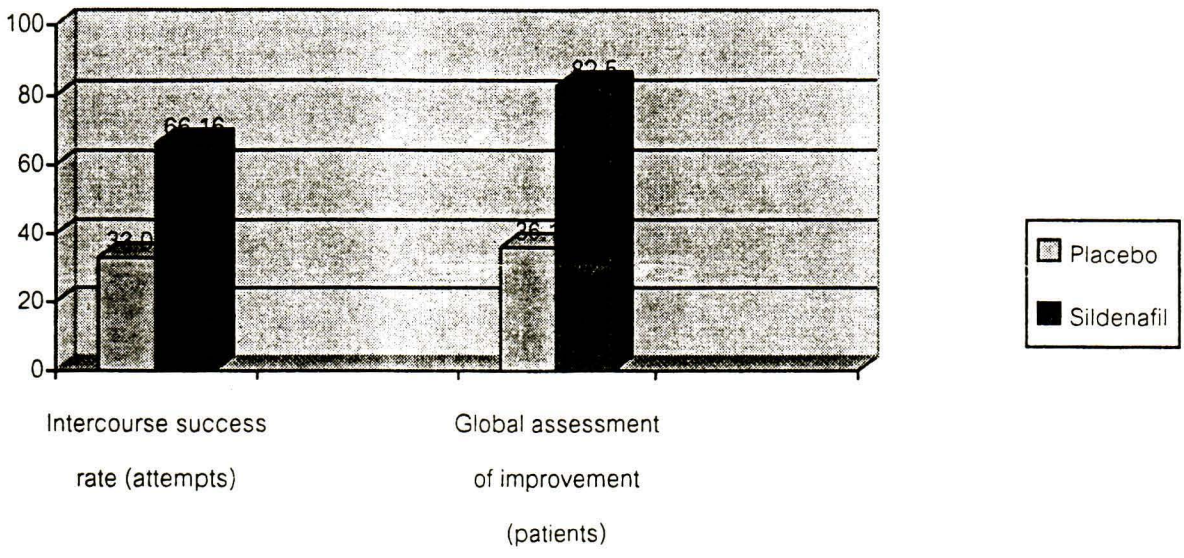

Fig. 4. Percentages of attempts at intercourse rated as successful (from available data recorded in patients' event log) and percentages of patients rating their erections as improved (as assessed *via* the global efficacy question) following administration of sildenafil or placebo for 12 weeks. *p = 0.0001 *versus* placebo.

fied according to the COSTART system. Adverse events considered by the investigators to be treatment-related occurred in 19 patients (30.2%) receiving sildenafil and 7 (11.3%) receiving placebo. In the sildenafil group, the most commonly encountered treatment-related adverse events were vasodilatation (flushing), headache, and dizziness, which occurred in 14.6 per cent, 6.3 per cent and 6.3 per cent of patients, respectively. Visual abnormalities and rhinitis were noted in a smaller number of patients (Table 2). All adverse events with sildenafil were mild in nature.

No patient receiving sildenafil had a serious treatment-related adverse event. Three patients receiving sildenafil had adverse events that required dose reductions; these were mild headache in two patients and a visual disturbance (orange patch of color from lamp) in one. There were no reports of priapism.

Laboratory results

Clinical laboratory test data were available for 110 patients (58 sildenafil, 52 placebo). None was required to discontinue treatment due to laboratory test abnormalities, and the median changes from baseline showed no clear patterns to suggest a relationship between sildenafil and any laboratory test parameter. Among patients who had normal baseline values, only three significant laboratory abnormalities were recorded in the sildenafil group; these were raised levels of eosinophils (> 1.5 x upper limit of normal (ULN), total bilirubin (> 1.5 x ULN) and blood urea nitrogen (> 1.3 x ULN), which occurred in one patient (1.7%) each. In comparison, four significant laboratory abnormalities were recorded in 2 patients receiving placebo.

DISCUSSION

Erectile dysfunction is commonly associated with aging and with various medical conditions such as diabetes mellitus, cardiovascular disease, renal and hepatic failure, neurological disease, certain drugs and types of surgery, pelvic or spinal cord trauma, and 'performance' anxiety[11,23,24]. Its prevalence in Thailand is 37.5 per cent in the 40-70 year-old group[20]. As with other Asian populations, erectile dysfunction is vastly undetected in the Thai population due to reluctance among sufferers to seek medical advice.

This reluctance is often due in part to embarrassment, to numerous myths about the condition that arise from cultural beliefs, and also to a lack of awareness among both patients and doctors of the availability of effective therapies efficacy assessment question concerning improvement in erections. The

Table 2. Numbers of patients receiving sildenafil and placebo who experienced adverse event the 12-week study period (all-cause and treatment-related events).

Adverse Events	Sildenafil group (n = 63)				Placebo group (n = 62)			
	All-cause ≈	%	Treatment-related‡	%	All-cause ≈	%	Treatment-related‡	%
All adverse events	23	36.5	19	30.2	21	33.9	7	11.3
Cardiovascular events (total)	12	19	9	14.3	9	14.5	1	1.6
Vasodilatation (flushing)	9	14.3	9	14.3	1	1.6	1	1.6
Abnormal EKG	2	3.2	0	0	2	3.2	0	0
Hypotension	1	1.6	1	1.6	0	0	0	0
Cardiovascular disorder	1	1.6	0	0	0	0	0	0
Body as a whole events (total)	6	9.5	6	9.5	3	4.8	3	4.8
Headache	4	6.3	4	6.3	3	4.8	3	4.8
Back pain	1	1.6	1	1.6	1	1.6	1	1.6
Facial edema	1	1.6	1	1.6	0	0	0	0
Respiratory system events (total)	3	4.8	3	4.8	0	0	0	0
Rhinitis	3	4.8	3	4.8	0	0	0	0
Nervous system events (total)	5	7.9	4	6.3	4	6.3	3	4.8
Dizziness	4	6.3	4	6.3	3	4.8	3	4.8
Insomnia	1	1.6	0	0	0	0	0	0
Special senses events (total)	3	4.8	3	4.8	0	0	0	0
Abnormal vision	6	4.6	5	3.8	0	0	0	0
Ear disorders	2	3.2	2	3.2	0	0	0	0
Musculoskeletal events (total)	1	1.6	1	1.6	0	0	0	0
Myalgia	1	1.6	1	1.6	0	0	0	0

≈ Adverse events recorded regardless of a suspected relationship to the study medication.
‡ Adverse events judged by the investigator to be treatment-related.

reluctance highlights the need for an effective agent that is simple to use, does not interfere with the spontaneity of the sexual relationship, and has minimal adverse effects. In view of published reports documenting the efficacy and/or safety of sildenafil in Western populations with erectile dysfunction[10-15,25], its safety in the local Thai population is of considerable interest and underlines the drug's expanding role in erectile dysfunction management.

In terms of safety, the presented findings confirm those in Western populations[25] in demonstrating that sildenafil is well-tolerated in Thai men, with a low rate of dose reduction or discontinuation due to adverse events. All of the treatment-related adverse events that occurred from the drug were mild in nature. Consistent with its known pharmacological effects, vasodilatation (flushing), headache, and dizziness were the most common adverse events, while rhinitis, visual disturbances, and myalgia were less common. No instances of priapism or other serious adverse events were observed during the 12-week investigation.

The absence of serious safety concerns in the presented patients mirrors the findings of a clinical safety overview of 28 Phase II/III studies with sildenafil conducted in Western populations[25]. In the pooled analysis of all Phase II and III studies, occurrence rates of myocardial infarction or other serious cardiovascular events did not increase in either the short- or long-term studies reviewed. Other than flushing, the incidence of adverse cardiovascular events in the 18 placebo-controlled studies was 3.0 per cent with sildenafil and 3.5 per cent with placebo, and the vast majority of these events were mild or moderate in nature[25]. No evidence of a significant treatment effect on blood pressure or heart rate was observed either in the present study in Thai patients or in the overview analysis of Phase II/III studies with sildenafil.

The tolerability of sildenafil in men receiving antihypertensive therapy is also of interest in view of the frequency with which erectile dysfunction and hypertension are likely to coexist. As in the overview analysis[25], many of the presented patients

were also taking antihypertensive medications, and tolerability in these patients was comparable to that in men who were not receiving antihypertensive therapy. However, in other studies, coadministration of sildenafil with organic nitrate drugs has been found to result in clinically significant decreases in blood pressure, and sildenafil is consequently contraindicated in men receiving nitrates or nitric oxide donor agents[25,26].

Only one of the presented patients (1.6%) experienced a visual abnormality. This adverse event, which was reported in 3 per cent of patients in the safety overview of studies in Western populations, may be related to a weak inhibitory effect of the drug on phosphodiesterase type 6, which is present in the retina and plays a role in the visual transduction pathway[25]. A recent study in 5 healthy volunteers showed that sildenafil doses of 100 mg had no effect on visual acuity, visual field, color vision, or intraocular pressure, but decreased the a-wave and b-wave amplitude in the electoretinogram (ERG) over a period of less than 6 hours[27]. The use of sildenafil does not in any way increase the risk of retinal changes. However, as there is no experience of use in individuals with rare genetic phosphodiesterase defects, it is advised that such individuals do not take the drug[28].

The authors have shown that a flexible dose regimen of sildenafil ranging from 25 to 100 mg taken one hour prior to anticipated sexual activity is effective in improving the sexual functioning of Thai men with erectile dysfunction of organic, psychogenic, or mixed origin, as evaluated by the patients' own assessments in their own environments.

Both the primary and secondary efficacy variables used in the present study showed significantly greater treatment effects for sildenafil in comparison with placebo. The only IIEF parameters that did not show a significant difference between the two groups were the number of attempts at sexual intercourse, the frequency of sexual desire, the level of sexual desire, and the satisfaction with the sexual relationship. Data from patients' event logs showed that the mean proportion of successful attempts at intercourse was more than doubled by sildenafil in comparison with placebo (67.37% of attempts *versus* 33.06%; $p = 0.0001$).

The present results in Thai men are similar to those reported in Western populations, with improvements in the ability to achieve and maintain erections sufficient for penetration and/or for the 5 IIEF domains being comparable to those achieved in double-blind, placebo-controlled studies conducted in the US and UK[10,12,13]. The authors employed a flexible dose schedule of sildenafil, allowing for increases up to 100 mg for lack of efficacy or reductions to 25 mg for lack of tolerability. The safety profile of sildenafil in Thai men reflects the same worldwide pattern and is similar to postmarketing findings obtained from over 16.4 million sufferers worldwide.

SUMMARY

The results of this randomized, double-blind, placebo-controlled, flexible-dose study conducted at 4 centers in Thailand indicate that sildenafil is an effective and safe oral treatment for Thai men with erectile dysfunction of organic, psychogenic, or mixed etiology. Both the primary and secondary efficacy variables evaluated showed statistically significant treatment effects for sildenafil in comparison with placebo. This included the frequency of penetration and maintenance of an erection following penetration, the 4 separate IIEF domains of sexual functioning (erectile function, orgasmic function, intercourse satisfaction, overall satisfaction), the percentage of successful attempts at intercourse, and global improvements in erections. Sildenafil was also well tolerated, and all adverse effects were mild in nature. Vasodilatation (flushing), headache, and dizziness were the most common events, reflecting the drug's pharmacologic activity.

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APPENDIX

Members of the ASSESS-2 (Asian Sildenafil Efficacy and Safety Study, # 2) Group in Thailand are :

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REFERENCES

1. Wagner G, Saenz de Tejada I. Update on male erectile dysfunction. BMJ 1998; 316: 678.
2. Linet OI, Ogrine FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. N Engl J Med 1996; 334: 873.
3. Padma-nathan H, Hellstrom WJ, Kaiser FE, et al. Treatment of men with erectile dysfunction with transurethral alprostadil. Medicated Urethral System for Erection (MUSE) Study Group. N Engl J Med 1997; 336: 1.
4. Morales A, Heaton JP, Johnston B, Adams M. Oral and topical treatment of erectile dysfunction. Present and future. Urol Clin North Am 1995; 22: 879.
5. Reid K, Surridege DH, Morales A, et al. Double-blind trial of yohimbine in treatment of psychogenic impotence. Lancet 1987; 2: 421.
6. Meinhardt W, Schmitz PI, Kropman RF, de la Fuente RB, Lychklama a Nejeholt AA, Zwartendijk J. Trazodone, a double blind trial for treatment of erectile dysfunction. Int J Impot Res 1997; 9: 163.
7. Montorsi F, Strambi LF, Guazzoni G, et al. Effect of yohimbine-trazodone on psychogenic impotence: A randomized, double-blind, placebo-controlled study. Urology 1994; 44: 732.
8. Becker AJ, Stief CG, Machtens S, et al. Oral phentolamine as treatment for erectile dysfunction. J Urol 1998; 159: 1214.
9. Boolell M, Allen MJ, Ballard SA, et al. Sildenafil : An orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. Int J Impot Pes 1996; 8: 47.
10. Goldstein L, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicher PA. for the Sildenafil Study Group: Oral sildenafil in the treatment of erectile dysfunction. N Engl J Med 1998; 338: 1397.
11. Boolell M, Gepi-Attee S, Gingell JC, Allen MJ. Sildenafil, a novel effective oral therapy for male erectile dysfunction. Br J Urol 1996; 18: 257.
12. Lue TF and the Sildenafil Study Group. Long-term efficacy and safety of sildenafil (Viagra™) : A 6-month, randomized, double-blind, placebo-controlled study in men with erectile dysfunction (ED). (Abstract). Int J Impot Res 1997; 9 (Suppl 1): S46.
13. Hodges M, Hargreaves C, Smith MD and the Multicentre Study Group. Sildenafil (Viagra™), an oral treatment for erectile dysfunction (ED): A 12-week, double-blind, placebo-controlled study. (Abstract). Int J Impot Res 1997; 9 (Suppl 1): S46.
14. Padma-Nathan H, Steers WD, Wicker PA. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction : A double-blind, placebo-controlled study of 329 patients. Sildenafil Study Group. Int J Clin Pract 1998; 52: 375.
15. Marks LS, Duda C, Dorey FJ, Macairan ML, Santos PB. Treatment of erectile dysfunction with sildenafil. Urology 1999; 53: 19.
16. Price DE, Angell JC, Gepi-Attee S, Wareham K, Yates P, Boolell M. Sildenafil study of a novel

oral treatment for erectile dysfunction in diabetic men. Diabet Med 1998; 15: 821.
17. Derry FA, Dinsmore WW, Fraser M, et al. Efficacy and safety of oral sildenafil (Viagra) in men with erectile dysfunction caused by spinal cord injury. Neurology 1998; 51: 1629.
18. Fava M, Rankin MA, Alpert JE, Nierenberg AA, Worthington JJ. An open trial of oral sildenafil in antidepressant-induced sexual dysfunction. Psychother. Psychosom 1998; 67: 328.
19. Zippe CD, Kedia AW, Kedia K, Nelson DR, Agarwal A. Treatment of erectile dysfunction after radical prostatectomy with sildenafil citrate (Viagra). Urology 1998; 52: 963.
20. Thai Erectile Dysfunction Epidemiologic Study Group. An epidemiologic study of erectile dysfunction in Thailand (part 1: Prevalence). J Med Assoc Thai 2000; 83: 872
21. NIH Consensus Conference. NIH Consensus Development Panel on Impotence. JAMA 1993; 270: 83.
22. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF) : A multidimensional scale for assessment of erectile dysfunction. Urology 1997; 49: 822.
23. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosexual correlates : Results of the Massachusetts male aging study. J Urol 1994; 151: 54.
24. Lim PH, Ng FC. Erectile dysfunction in Singapore men: Presentation, diagnosis, treatment and results. Ann Acad Med Singapore 1993; 21: 248.
25. Morales A, Gingell C, Collins M, Wicker PA, Osterloh IH. Clinical safety of oral sildenafil citrate (Viagra™) in the treatment of erectile dysfunction. Int J Impot Res 1998; 10: 69.
26. Cheitlin MD, Hutter Jr AM, Brindis RG, et al. Use of sildenafil (Viagra) in patients with cardiovascular disease. Circulation 1999; 99: 168.
27. Vobig MA. Retinal side-effects of sildenafil. Lancet 1999; 353: 375.
28. Zrenner E. No cause for alarm over retinal side-effects of sildenafil. Lancet 1999 353: 340.

ประสิทธิผล และความปลอดภัยของยาซิลเดนาฟิลในชายไทยที่มีปัญหาหย่อนสมรรถภาพทางเพศ†

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วัตถุประสงค์ : เพื่อประเมินประสิทธิผล และความปลอดภัยของซิลเดนาฟิลซิเตรต (ไวอากร้า) ในชายไทยที่มีปัญหาหย่อนสมรรถภาพทางเพศซึ่งเกิดจากหลากหลายสาเหตุและเป็นมานานกว่า 6 เดือน

วิธีการศึกษา : ทำการคัดเลือกผู้ป่วยแบบสุ่ม จำนวน 125 ราย ซึ่งมีอายุมากกว่า 18 ปี ในโรงพยาบาล 4 แห่ง คัดเลือกเพื่อรับยาซิลเดนาฟิลซิเตรต จำนวน 63 ราย (ขนาดเริ่มต้น 50 มิลลิกรัม ซึ่งอาจจะปรับเพิ่มเป็น 100 มิลลิกรัมหรือลดเป็น 25 มิลลิกรัม แล้วแต่ประสิทธิผลและความทนต่อยา) หรือเพื่อรับยาหลอก จำนวน 62 ราย เวลาที่รับประทานยาคือเมื่อมี "ความต้องการ" และรับประทานประมาณ 1 ชั่วโมงก่อนมีกิจกรรมทางเพศ ช่วงระยะเวลาทำการศึกษาคือ 12 สัปดาห์

ประสิทธิผลประเมินโดย ให้ผู้ป่วยตอบแบบสอบถาม International Index of Erectile Function (IIEF) แบบสอบถามบันทึกประจำวันเรื่องกิจกรรมทางเพศและแบบสอบถามเรื่องการประเมินประสิทธิผลโดยรวมต่อการแข็งตัว

ผลการศึกษา : พบว่ากลุ่มผู้ป่วยที่ได้รับซิลเดนาฟิล มีคะแนนที่ได้จากการประเมินโดย แบบสอบถามทั้ง 3 ประเภทเกี่ยวกับการแข็งตัว กิจกรรมทางเพศและความพึงพอใจโดยรวม มากกว่ากลุ่มผู้ป่วยที่ได้รับยาหลอกในทุกกลุ่มคำถาม อย่างมีนัยสำคัญทางสถิติ ยกเว้นเรื่องความต้องการทางเพศ ซึ่งไม่พบความแตกต่างระหว่าง 2 กลุ่ม โดยมีอัตราความสำเร็จในการมีเพศสัมพันธ์ในกลุ่มผู้ป่วยที่ได้ซิลเดนาฟิลร้อยละ 66.16 เทียบกับผู้ป่วยที่ได้รับยาหลอกร้อยละ 33.05 และผลการประเมินประสิทธิภาพของการแข็งตัวโดยรวมพบว่า ในผู้ป่วยกลุ่มที่ได้ซิลเดนาฟิล มีการแข็งตัวที่ดีขึ้นร้อยละ 82.5 เทียบกับกลุ่มที่ได้รับยาหลอกร้อยละ 36.2 ซึ่งแตกต่างอย่างมีนัยสำคัญทางสถิติ

เหตุการณ์ไม่พึงประสงค์ซึ่งเกี่ยวเนื่องกับการใช้ยา พบในผู้ป่วยที่ได้รับยาซิลเดนาฟิล 19 ราย (ร้อยละ 30.2) และพบในผู้ป่วยที่ได้รับยาหลอก 7 ราย (ร้อยละ 11.3)

เหตุการณ์ไม่พึงประสงค์ที่พบบ่อยที่สุด คือ อาการหน้าแดง ปวดศีรษะ และมึนงง ซึ่งเกิดร้อยละ 14.3, 6.3 และ 6.3 ตามลำดับ ซึ่งเหตุการณ์ที่เกิดขึ้นทั้งหมดเป็นเพียงอาการเล็กน้อยเท่านั้น

สรุปผล : ยาซิลเดนาฟิล ปลอดภัยและมีประสิทธิผลในการรักษาผู้ป่วยชายไทยที่มีปัญหาความผิดปกติในการแข็งตัวของอวัยวะเพศ ข้อมูลเรื่องประสิทธิผลนี้ในการศึกษาเหมือนกับที่เคยมีรายงานมาก่อนในประชากรตะวันตก

คำสำคัญ : ความผิดปกติในการแข็งตัวของอวัยวะเพศ, ซิลเดนาฟิล, ประสิทธิผล, ความปลอดภัย

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