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Original Article

Effect of sildenafil on erectile dysfunction and improvement in the quality of sexual life in China: a multi-center study

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Abstract: Background: Erectile dysfunction (ED) is a common medical condition in middle-aged and elderly men; however, large-scale and multi-center epidemiologic studies about the treatment effects on ED in China are lacking. Objective: To elucidate the efficacy and safety of a phosphodiesterase type 5 inhibitor (PDE5-i) in the treatment of men with ED in China. Methods: Patients clinically diagnosed with ED from 53 andrology centers in 15 metropolitan areas in China who were willing to undergo treatment for ED were enrolled in the study. Each participant received 4 weeks of unique PDE5-i treatment, and completed the following forms (International Index of Erectile Function score 5 [IIEF-5], the Erection Hardness Score [EHS], Self-Esteem and Relationship [SEAR], and SF-36 of Health Related Quality of Life). Pre-and post-treatment data were compared using descriptive analysis. Results: A total of 1956 ED patients were included in this study; 1922 patients provided valid questionnaires for analysis. Four weeks of sildenafil treatment was considered effective and safe. Specifically, the IIEF-5 sores (11.30 ± 3.7 vs. 20.02 ± 5.1, $P < 0.05$), EHS levels (99.1% patients increases to level 3 or 4), and the SEAR scores (32.5 vs. 55.1, $P < 0.05$) were significantly improved compared to baseline. Sildenafil therapy also significantly improved the satisfaction, enjoyment, and frequency of sexual attempts and sexual activity, as well as physical vigor and mental health scores. Conclusion: The present study provides direct evidence regarding the efficacy and safety of sildenafil therapy in a large sample of Chinese men with ED, thus verifying that sildenafil improved the symptoms and quality of sexual life.

Keywords: Erectile dysfunction, sildenafil, sexual quality, China

Introduction

Erectile dysfunction (ED), which is defined as an inability to attain or maintain an erection sufficient for satisfactory sexual performance, is a common disease in middle-aged and elderly males, with an estimated prevalence across all ages ranging from 10%-20% [1, 2]. ED affects the quality of life and psychological well-being of patients. Even though different districts have reported different incidences of ED, large-scale and multi-center epidemiologic studies are lacking in China [3].

As the first-line treatment for ED, phosphodiesterase type 5 inhibitors (PDE5-is) are used worldwide, and the efficacy of PDE5-is has been confirmed. PDE5-is are typically administered orally, and the overall efficacy is reported to be 60%-70% [4]; however, approximately one-third patients have a poor response to PDE5-is, and these patients are referred to as "difficult to treat" [5]. The reasons for a poor response to therapy may be related to race, population, education, the clinician, or physical problems. For some patients, severe neurologic damage, vascular disease, and diabetes mellitus are among the main reasons for a poor response to PDE5-is. Sildenafil is the most common PDE5-I used to treat ED in outpatients in China and elsewhere. While several studies [4, 5] have reported the therapeutic effects of sildenafil, an over-

Table 1. Sexual parameters before and after Sildenafil treatment

Variables	Before	After	*P*
IIEF-5 score	11.30 (3.7)	20.02 (5.1)	0.01*
ED severity (EHS)			
Grade I	190 (9.9)	6 (0.3)	0.00**
Grade II	915 (47.6)	12 (0.6)	0.00**
Grade III	805 (41.9)	584 (30.4)	0.02*
Grade IV	12 (0.6)	1320 (68.7)	0.00**
Success insertion rate	46%	93%	0.02*
Frequency of sexual attempts per month			
0	103 (5.4%)	4 (0.2%)	0.01*
1-2	440 (22.9%)	156 (8.1%)	0.03*
3-4	709 (36.9%)	688 (35.8%)	0.42
5-6	350 (18.2%)	513 (26.7%)	0.03*
7-10	257 (13.4%)	432 (22.5%)	0.02*
> 11	63 (3.3%)	129 (6.7%)	0.02*
Frequency of sexual activity per month			
0	436 (22.7%)	11 (0.6%)	0.01*
1-2	828 (43.1%)	198 (10.3%)	0.01*
3-4	411 (21.4%)	750 (39%)	0.02*
5-6	156 (8.1%)	496 (25.8%)	0.02*
7-10	83 (4.3%)	375 (19.5%)	0.03*
> 11	8 (0.4%)	92 (4.8%)	0.01*
Sexual time			
< 1 min	114 (5.8)	6 (0.3)	0.01*
1-2 min	270 (14.1)	13 (0.7)	0.00**
2-3 min	374 (19.5)	83 (4.3)	0.02*
3-5 min	724 (37.7)	488 (25.4)	0.02*
> 5 min	440 (22.9)	1332 (69.3)	0.01*

IIEF-5, the International Index of Erectile Function score 5; EHS, the Erection Hardness Score; *P < 0.05, **P < 0.01.

all analysis involving a large, multi-center sample of ED patients treated with PDE5-is has not been conducted in China.

In the present study we collected questionnaires from ED patients treated with sildenafil at 53 andrology centers in 15 metropolitan areas in China. Detailed data were collected from ED patients before and after treatment. The results revealed the response and effect of PDE5-i therapy in Chinese ED patients and provided a theoretical basis for standardization of future treatment in China.

Subjects and methods

Subjects

The present study was initiated by the Chinese Andrological Association. In 2011, ED patients seeking oral therapy at local andrology clinics were invited to participate in the study. Patients clinically diagnosed with ED from 53 andrology centers in 15 major cities (Beijing, Shanghai, Guangzhou, Nanjing, Wuhan, Hangzhou, Dalian, Shenyang, Jinan, Taiyuan, Xuzhou, Qingdao, Weihai, Lanzhou, and Shijiazhuang) were included in this study. Patients with major illnesses (poorly controlled diabetes mellitus or untreated proliferative diabetic retinopathy, a history of stroke or myocardial infarction, or a life-threatening arrhythmia), and patients taking nitrates or anticoagulants were excluded. All the trials were approved by local independent review boards and all patients provided written informed consent.

Treatment and follow-up

Sildenafil (Viagra, Pfizer Inc., NY, USA) is the most commonly used medication for ED treatment in China; the therapeutic dose ranges from 25 to 100 mg in different centers. Throughout the present study, patients received sildenafil treatment only (11.2%, 14.5%, and 74.2% of patients received 25 mg, 50 mg, and 100 mg > q24 h, respectively). Patients were required to take sildenafil as prescribed. Treatment was continued for 4 weeks after administration of the first dose of sildenafil. Before and after treatment, patients completed questionnaires which included the following instruments: International Index of Erectile Function score 5 (IIEF-5); Erection Hardness Score (EHS); Self-Esteem and Relationship (SEAR); and SF-36 of Health Related Quality of Life (HRQoL). It is widely acknowledged that IIEF-5, EHS, SEAR, and SF-36 are reliable tools for assessing ED, and are also commonly used in studies evaluating the efficacy of therapies for ED [6-8]. The SF-36 of HRQoL was used to evaluate the general health, vitality, and mental health of the subjects.

Table 2. General health conditions before and after Sildenafil treatment

Variables	Before	After	*P*
SEAR	32.5	55.1	0.04*
General health condition	2.48 ± 0.86	3.92 ± 1.00	0.16
Physical vigor	10.94 ± 3.41	17.14 ± 3.41	0.03*
Mental condition	17.59 ± 3.42	26.30 ± 6.31	0.03*

SEAR, the Self-Esteem and Relationship; *P < 0.05.

Statistical analysis

Data were analyzed with SPSS13.0 software (SPSS Inc., Chicago, IL, USA). Data are expressed as the mean and standard deviation (mean ± SD). For continuous data, overall differences were tested by an independent sample *t*-test between groups. Categorical data and significance of differences were determined using a chi-square test. A $P < 0.05$ was considered statistically significant.

Results

General conditions of the subjects

A total of 1922 valid questionnaires were collected in the current study. The ages of patients ranged from 30 to 72 years (average, 40 y). Among the patients, 91.2% had a disease duration < 5 y, 60% had a history of smoking and consuming alcohol, and 57.2% had > 1 co-morbidities (e.g., prostatitis, benign prostate hyperplasia, hypertension, hyperlipidemia, or diabetes mellitus). Before treatment, as reflected by the IIEF-5 score, 83% patients had mild-to-moderate ED. Among all of the participants, 83.3% attempted intercourse < six times per month (3.3%, > ten times per month; 13.4%, 7-10 times; 18.2%, 5-6 times; 36.9%, 3-4 times; 22.9%, 1-2 times; 5.4%, zero), 87.2% entered the vagina < 4 times per month (most often, 1-2 times with a success rate < 50%), and 87.1% ejaculated < 5 min from entering the vagina (most often, 3-5 min). Altogether, 97% patients were not satisfied with the quality of their sexual life, while 75% were not satisfied with their general health status. Of the study participants, 55% had never used any medications for ED.

Sildenafil effects on ED symptoms

After 4 weeks of sildenafil treatment, the overall ED symptoms of the patients were improved (**Table 1**). The average IIEF-5 score was significantly improved (increased from 11.30 ± 3.7 to 20.02 ± 5.1, P < 0.05). Greater than 40% of patients recovered to a normal level based on the IIEF-5 score, and 98.4% of patients reported that their erectile function had improved.

As shown by EHS grading (grading I-IV represents an increase in hardness), the overall penile hardness in the patients was significantly improved. The percentage of patients with EHS grade I, II, and III decreased from 9.9% to 0.3%, 47.6% to 0.6%, and 41.9% to 30.4%, respectively, while the percentage of patients with EHS grade IV increased from 0.6% to 68.6%. A total of 99.1% patients enjoyed erectile hardness better than EHS grade III.

The successful vaginal insertion rate increased from 46% to 93% (P < 0.05). Sildenafil treatment improved the satisfaction rate (complete or quite satisfied) in approximately 98% of patients. The time from vaginal insertion to ejaculation was also improved. Patients who engaged in intercourse > 5 min were increased from 12.9% to 69.3%.

Sildenafil effects on general health conditions

In addition to the sexual relationship, the self-confidence and self-esteem of the subjects were also ameliorated following PDE5-i therapy, as indicated by the higher SEAR score (from 32.5 to 55.1, $P < 0.05$; **Table 2**).

The SF-36 was assessed to determine the general health of the patients. General health was divided into 5 sub-grades (0: bad, 1: normal, 2 well, 3: better, 4: very well). The general health of patients was improved by treatment (from 2.48 to 3.92, $P > 0.05$). In addition, physical vigor and mental status were significantly improved (**Table 2**).

Discussion

Sildenafil, a PED5-i, has a long history of use worldwide. Sildenafil also has the advantage of slowing corpora cavernosa aging (apoptosis) and improving spermatogenesis by acting upon endothelial cells and improving the microcirculation [9]. In the present study, all of the patients accepted sildenafil therapy for 4 weeks. Because of different sensitivities and tolerance to the side effects of drugs, the dose of silde-

nafil ranged from 25-100 mg in different centers; specifically, 11.2%, 14.5%, and 74.2% of the patients were prescribed 25 mg, 50 mg, and 100 mg, respectively.

The age of the ED patients was much younger (between 30 and 50 y) in the present study, while in most international studies the age of ED patients was between 40 and 70 y. We speculate that this age difference is due to the traditional concept in China that a substantial proportion of patients with ED tend to avoid treatment, thus most ED patients seeking treatment are younger or have more severe symptoms. Older patients are more reserved than younger patients, and elderly patients prefer to live a longer life than to improve erectile function. In the current study, elderly patients (> 60 y) accounted for only 4.2% of the study population. Therefore, the safety and efficacy of sildenafil among elderly Chinese patients warrants a stratified analysis.

In the present study, we found that > 60% of patients was exposed to smoking and alcohol consumption, and > 40% had prostatitis. Patients diagnosed with prostatitis underwent rigorous treatment, but failed to be cured before PDE5-i therapy. In contrast, patients with hypertension or vascular lesions underwent less rigorous treatment. This phenomenon also coincided with the age structure of the patients.

Several possibilities might explain why the treatment efficacy in the present study was much better than other reports [10, 11]. First, our previously published study proved that the longer the duration of ED, the more severe the ED because the various co-morbidities aggravate the symptoms of ED [12]. In the present study, we showed that > 90% of the patients had a history of ED < 5 y duration, and > 60% of the patients had fewer co-morbidities (≤ 2). Second, during the course of follow-up, patients failing therapy often sought other treatments and declined to provide information to the current study researchers. We speculate that this also contributed to the higher improvement rate. Third, the age of ED patients in the current study was younger than most studies. The patients' notion that ED is an irreversible trend with age and that it is not necessary to take a medication excluded many older patients [13].

The present study is the first multi-center study involving the efficacy of PDE5-i treatment for ED in China. The results have confirmed the reliability of sildenafil and have also provided authoritative data. Further studies are needed regarding the optimal dose of sildenafil and the optimal timing for treatment in Chinese men with ED. Elderly patients always have a low serum androgen level, and combination therapy with androgen may result in a better effect [14]. Although the literature suggests that sildenafil lowers direct costs compared with other PDE5-is and has a favorable cost-effective profile [15], evaluating the feasibility of a smaller dose may be more appropriate for patients. As described above, 30%~35% of patients fail to respond to standard therapy and may require more effective and potent treatment. It has been reported that tadalafil has a longer half-time and a more lasting effect [16, 17]. A subsequent study showed that 2.5-5 mg of tadalafil might play an active role because it broke the classical on-demand property of traditional PDE5-i drugs [5]. Thus, further studies on the effects of other PDE5-is in Chinese ED patients are needed.

There were several limitations in the present study. First, selection bias is inevitable for the outpatients enrolled in this study, as some patients with poor treatment effects were automatically disenrolled. Second, the placebo control group was not set, possibly resulting in an exaggerated therapeutic effect of sildenafil. In addition, therapy for 4 weeks is relatively short for some indicators required for at least 1 month (e.g., the frequency of sexual activity and attempts). Third, it is important and more objective to include the feelings of female partners in evaluating the satisfaction and enjoyment of therapy [18].

In conclusion, sildenafil showed beneficial effects in Chinese ED patients. After 4 weeks of treatment, sildenafil significantly facilitated the sexual activity, self-confidence, mental status, and improved the quality of sexual life. With the advantage of low side effects and the convenience of administration, it is possible that Chinese ED patients can restore sexual function via medication.

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Disclosure of conflict of interest

None.

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