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·*Original Article*·

Treatment preferences in men with erectile dysfunction: an open label study in Korean men switching from sildenafil citrate to tadalafil

Tai Young Ahn[1], Sung Won Lee[2], Sae-Woong Kim[3], Dae Yul Yang[4], Nam Cheol Park[5], Kweon-Sik Min[6], Kwangsung Park[7], Jae-Seung Paick[8], Yulia Dyachkova[9], Trisha Dwight[10], Myung-Sea Luke Lee[11]

[1]Asan Medical Centre, Seoul 138-736, Korea; [2]Samsung Medical Centre, Seoul 135-710, Korea; [3]Youido St Marys Hospital, Seoul 150-713, Korea; [4]Kang Dong Sacred Heart Hospital, Seoul 134-701, Korea; [5]Pusan National University Hospital, Pusan 602-739, Korea; [6]Pusan Inje University Paik Hospital, Pusan 614-735 , Korea; [7]Chonnam National University Hospital, Gwangju 501-757, Korea; [8]Seoul National University Hospital, Seoul 110-744, Korea; [9]Area Medical Centre Vienna, Eli Lilly Austria, Sydney A-1030, Australia; [10]Intercontinental Information Sciences, Eli Lilly Australia, Sydney 2113, Australia; [11]Eli Lilly Korea, Seoul 135-280, Korea.

Abstract

Aim: To evaluate patient preferences for sildenafil citrate or tadalafil (PDE-5 inhibitors available for the treatment of erectile dysfunction [ED]) and assess potential reasons for these preferences. **Methods:** This open-label study was conducted on Korean men taking sildenafil, at least 6 weeks prior to study entry, for ED. Following screening, patients continued sildenafil treatment for 4 weeks, then after a 1-week washout period, switched to tadalafil for 8 weeks. Patients then continued with their treatment of choice during an extension phase. Psychosocial factors (time concern, spontaneity, sexual self-confidence) were evaluated using Psychological and Interpersonal Relationship Scales (PAIRS), while timing of dose to sexual attempt patterns were assessed from patient diaries. **Results:** The present study enrolled 160 Korean men (mean age 55 years) with prior median sildenafil use of 585 days. During the extension phase, 73.7% of patients elected to take tadalafil, whereas 26.3% chose sildenafil ($P < 0.001$). After switching from sildenafil to tadalafil, mean PAIRS time concern scores decreased from 2.54 to 2.42 ($P = 0.002$), with no statistically significant differences observed between the sildenafil and tadalafil assessment phases in sexual spontaneity and self-confidence scores. Sexual attempts made > 4 h to ≤ 36 h post-dose occurred in 4.5% of patients during the sildenafil assessment phase compared with 17.5% during the tadalafil assessment phase. **Conclusion:** After experiencing both sildenafil and tadalafil, the majority of patients exhibited a preference for tadalafil. This preference might be influenced by psychosocial factors, such as decreased time concerns, and a broader window of opportunity available for sexual activity. *(Asian J Androl 2007 Nov; 9: 760–770)*

Keywords: erectile dysfunction; tadalafil; sildenafil citrate; Psychological and Interpersonal Relationship Scales; preference

Correspondence to: Dr Trish Dwight, Intercontinental Information Sciences (ICIS), Eli Lilly Australia Pty Limited, Level 1, 16 Giffnock Avenue, Macquarie Park NSW 2113, Australia.
Tel: +61-2-8874-5832 Fax: +61-2-8874-5733 E-mail: tdwight@lilly.com
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1 Introduction

Over 150 million men worldwide were estimated to have been affected by erectile dysfunction (ED) in 1995, with projected estimates of over 320 million by 2025 [1]. ED has been shown to have a negative impact on a patients' self-esteem, quality of life and interpersonal relationships, and has also been associated with increased age, diabetes, kidney disease, atherosclerosis, vascular disease and depression [2], although it is unclear as to whether ED is the initiating disorder or whether it arises as a result of these other underlying disorders.

Under normal conditions, cyclic guanosine monophosphate (cGMP) mediates relaxation of vascular smooth muscle to achieve erectile rigidity. Phosphodiesterase type 5 (PDE-5) is an enzyme that breaks down cGMP and thereby assists in promoting penile flaccidity [3]. Oral phosphodiesterase type 5 (PDE-5) inhibitors, such as sildenafil citrate (sildenafil), tadalafil, and vardenafil hydrochloride (vardenafil), prevent the breakdown of cGMP and thereby promote erectile responses to sexual stimulation. These oral pharmacotherapies are easier to administer and less invasive than other ED approaches, such as intracavernosal injections and penile implants [4]. All three PDE-5 inhibitors, approved for the treatment of ED, have been shown to be of similar efficacy and tolerability. However, compared to others in its class, tadalafil has an extended half-life (17.5 h compared with 4–5 h) [3], has been shown to be effective for up to 36 h post-dose [5], and food consumption does not affect its absorption [6].

The present study was conducted primarily to evaluate patient preferences for sildenafil or tadalafil for the treatment of ED in a cohort of current sildenafil users in Korea. Additionally, psychological outcomes, such as time concerns, spontaneity and sexual self-confidence, were assessed to determine whether these factors play a role in patient attitudes towards treatment types. Furthermore, timing of dose to sexual attempt patterns was assessed, in each treatment group, to determine whether experienced sildenafil patients change their behavior with new dosing instructions that suggest a broader window of opportunity from dose to sexual intercourse (while on tadalafil).

2 Materials and methods

2.1 Selection criteria

Men were eligible for the study if they were at least 18 years of age and had at least a 3-month history of ED (defined as a consistent change in the quality of erection that adversely affects the patient's satisfaction with sexual intercourse). Patients presenting with ED of any functional severity (mild, moderate or severe) and of any etiological classification (psychogenic, organic or mixed) were eligible for enrolment, with disease etiology and severity being defined subjectively according to each investigator's clinical opinion. Patients anticipating to have the same female sexual partner throughout the study and having had at least 6 weeks prior use of sildenafil (Pfizer, New York, USA), at a stable dose, were eligible for enrolment. The dose of sildenafil was determined by the patient and treating investigator. Patients were excluded from the study for the following reasons: presentation of ED associated with premature ejaculation or untreated endocrine disease; failure to achieve erection after pelvic surgery, including radical prostatectomy (except bilateral nerve-sparing); significant penile deformity or penile implant; clinically significant renal or hepatic insufficiency; poorly controlled diabetes (hemoglobin $A_{1c} > 13\%$); unstable cardiovascular diseases (such as unstable angina, recent myocardial infarction, or coronary intervention, evidence of congestive heart failure, new significant conduction defect, or uncontrolled hypertension); recent history of significant central nervous system injuries; retinitis pigmentosa; a history of HIV infection; or previous participation in a tadalafil study. Concomitant use of other therapies for ED was not allowed.

2.2 Study design

This open-label, single arm study encompassed eight study sites within Korea. The first patient visit occurred in June 2004, with the last patient visit occurring in June 2005. The institutional or ethical review board of each site approved the protocol and all patients provided written consent prior to enrolment. The study included six patient visits (Figure 1). At Visit 1, patients signed an informed consent document, were evaluated for study inclusion, medical history and demographics, and subjected to physical examination and clinical laboratory measurements. For a subsequent week of screening, they continued taking their own supply of sildenafil at their pre-study dose. This dose was fixed for all subsequent exposures (including the extension phase). If it was considered necessary to titrate the dose of study

medication after enrolment for any patient, they were discontinued from the study. This ensured optimal efficacy and tolerability of sildenafil was established prior to the assessment phase. At Visit 2, patients were provided with a supply of sildenafil for 4 weeks and a set of dosing instructions (sildenafil assessment phase). At Visit 3, patients were provided with a supply of 20 mg tadalafil (Eli Lilly and Company, Indianapolis, USA) for 4 weeks and a set of dosing instructions; they were told not to take any tablets for a 1-week period (washout period) and then to commence taking tadalafil for 4 weeks (tadalafil initiation phase). At Visit 4, patients were provided with another supply of 20 mg tadalafil and a set of dosing instructions (tadalafil assessment phase). At Visit 5, patients were given the opportunity to choose either sildenafil or tadalafil for treatment during an extension phase of 12 weeks; either treatment was dispensed accordingly. The study was completed at Visit 6.

2.2.1 Dosing instructions

For sildenafil, patients were given 12 doses in commercially available packaging, including the package insert (patient leaflet). In a set of additional dosing instructions derived from the current sildenafil label, they were instructed to take their pre-study dose of sildenafil with water approximately 1 h before sexual activity, and informed that the dose could be taken as early as 4 h before sexual activity and as late as 30 min before sexual activity. Patients were also instructed that a high fat meal might delay its onset of action.

For tadalafil, patients were provided with 12 doses (per treatment phase) of 20 mg tadalafil in a clinical trial packaging and a set of dosing instructions. Patients were instructed to take no more than one dose per day with water before the potential for sexual activity. They were told tadalafil was shown to be effective up to 24 h after dosing and, in many patients, as early as 30 min after dosing. Patients were advised to initiate sexual activity at various times after dosing to determine their own optimal window of responsiveness. At the time of study initiation, a decision was taken to instruct patients on a 24-h duration of action for tadalafil, even though it has previously been shown to be effective for up to 36 h. This was because, at that time, some country-specific product labels were approved for only 24-h duration.

For the extension phase, patients were dispensed 36

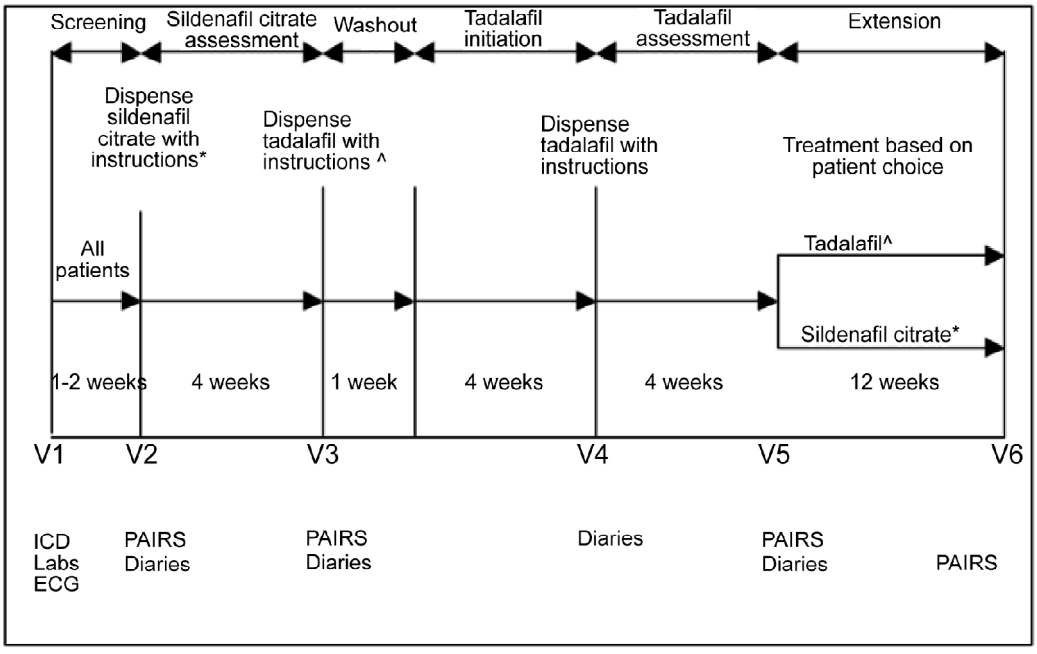

Figure 1. Study design. *sildenafil as pre-study dose; ^tadalafil as 20 mg dose; V, visit; ICD, informed consent document; ECG, electrocardiogram; PAIRS, Psychological and Interpersonal Relationship Scales.

doses of their chosen treatment, either sildenafil in commercially available packaging or bottles of tadalafil, and a set of treatment specific dosing instructions. Both medications were given as needed before sexual activity.

2.2.2 Outcomes and measures

The primary outcome was patient preference for ED treatment, which was measured by the proportion of patients electing (at Visit 5) to take sildenafil or tadalafil during the extension phase. Secondary outcomes included sexual encounter attributes (as measured by the Psychological and Interpersonal Relationship Scales [PAIRS]) and tolerability, and *post-hoc* analyses were performed to assess the time between dosing and sexual attempt.

PAIRS is a validated, self reported measure used to assess three conceptual domains: time concern, spontaneity and sexual self-confidence during sexual encounters (Table 1) [7]. PAIRS was given to patients at Visit 2 (prior to the sildenafil assessment phase), Visit 3 (after the sildenafil assessment phase), Visit 5 (after the tadalafil assessment phase) and Visit 6 (on completion of the study, after the extension phase) for the assessment of patient sexual encounter attributes. Dosing diaries and sexual attempt timing diaries were given to patients at Visit 2 (prior to the sildenafil assessment phase), Visit 3 (after the sildenafil assessment phase) and Visit 4 (prior to the tadalafil assessment phase). At Visit 5 (the beginning of the extension phase), only dosing diaries were dispensed. Diaries were collected and reviewed at Visits 3, 4, 5 and 6. Adverse event data and vital signs were assessed at all visits.

2.3 Statistical methods

2.3.1 General

All analyses included patients with baseline and at least one postbaseline measure. Safety summaries included all patients. All hypothesis testing was two-sided using a 0.05 level of significance and 95% confidence intervals. Analyses were conducted using the SAS statistical package version 8.02 for Windows (SAS Institute, Cary, NC, USA).

The proportion of patients electing to take sildenafil or

Table 1. Psychological and Interpersonal Relationship Scales (PAIRS) domain questions. Each question is measured using a 4-point scale: 1, strongly disagree; 2, disagree; 3, agree; 4, strongly agree. The patient's response to each specific question/domain is based on his experience over the past 4 weeks.

Time Concern Domain		
1.	The dating experience feels rushed when we are planning to have sex later.	
2.	I am very aware that if I wait too long after taking my medication, it may not work.	*Decreasing* scores
3.	Once I take my medication, I want to have sex as soon as possible.	in the Time Concern
4.	Dates feel programmed in order to have sex on schedule.	Domain indicate a
5.	My partner sometimes feels some pressure to have sex with me.	positive outcome.
6.	Sometimes I ruin the mood by having to worry about the time.	
7.	I find myself feeling hurried when I think we will have sex later on.	
8.	I find myself worrying whether my medication will wear off before I can use it.	
Spontaneity Domain		
1.	When we are alone before having sex, we can talk freely without feeling rushed.	*Increasing* scores in the
2.	We are able to be easygoing when we are out together.	Spontaneity Domain
3.	Before we have sex, I feel I can "go with the flow" with my partner when we are alone together.	indicate a positive
4.	When we will probably have sex later, we have time to be romantic and easygoing together.	outcome.
Sexual Self-Confidence Domain		
1.	I am able to have sex as I used to.	
2.	I feel very comfortable about my sexual ability.	*Increasing* scores in the
3.	I feel fantastic about my sex life.	Sexual Self-Confidence
4.	I am confident I can achieve an erection when the mood is right.	Domain indicate a
5.	I am confident that I can enjoy spontaneous sexual activity.	positive outcome.
6.	It is very easy to have fulfilling sexual intercourse.	

tadalafil during the extension phase was analyzed using a binomial proportion test; an exact 95% confidence interval for the percentage of patients selecting tadalafil was calculated.

2.3.2 PAIRS

The following domains from PAIRS (Table 1) were assessed prior to and during the extension phase: time concerns, spontaneity and sexual self-confidence. The mean of individual questions for a single patient was taken as the domain score for that visit (range 1–4). Unless stated otherwise, all scores are summarized by mean ± SD. Standard error of the mean is denoted as SEM.

For each PAIRS domain, the change from the sildenafil assessment phase (Visit 3) to the tadalafil assessment phase (Visit 5) was analyzed using linear mixed effects models adjusting for baseline score (Visit 2). The null hypothesis for this analysis was that there was no difference between PAIRS domain scores at Visit 3 compared to those at Visit 5. The change from the tadalafil assessment phase to the extension phase in PAIRS domain scores was analyzed using an analysis of covariance model with terms for treatment choice and baseline PAIRS score. The null hypothesis was that there was no difference between changes in PAIRS domain scores recorded by patients who preferred tadalafil compared with those who preferred sildenafil. *Post-hoc* analyses were also performed to investigate the null hypothesis that there was no difference in domain scores between preference groups at Visits 2 (baseline), 3 and 5.

2.3.3 Analyses of timing

Patients recorded the time of each dose taken and each sexual intercourse attempt between all visits except Visit 6. The duration of time between a dose and each subsequent intercourse attempt (prior to the next dose) was calculated in hours. As patients might have made several attempts between each visit, for each patient, the duration between dose and sexual intercourse attempt was summarized by median at each visit. The median was calculated because of the skewed distribution of data as it provides a more robust estimate of the centre of the measured values. Paired *t*-tests were used to compare the median time from dose to intercourse attempt, as well as the number of doses taken per week and the number of sexual intercourse attempts between visits. The proportion of sexual intercourse attempts occurring ≤ 4 h, > 4 h to < 8 h, ≥ 8 h to < 12 h, and ≥ 12 h post-dose were summarized for each study phase.

A cut-off point of 36 h was used for all summaries and analyses in the study to eliminate the potential effect of any outliers skewing the distribution for either study drug. This cut-off point was chosen because 36 h is the longest published duration of efficacy of a PDE-5 inhibitor for ED.

3 Results

3.1 Patient characteristics

Baseline clinical and demographic patient characteristics are outlined in Table 2. A total of 160 patients with ED from Korea were enrolled. All enrolled patients were of East/Southeast Asian origin, with the majority having a moderate severity of ED (68.8%), as assessed by the investigator. Patient age ranged from 32 to 75 years, with a mean of 55 years. The median duration of sildenafil use prior to enrolment was 585 days (range: 43–2 016 days), with the only doses of sildenafil used being 50 mg (45.6%) and 100 mg (54.4%).

Of the 160 patients enrolled, four (2.5%) did not complete the study. Of these, two patients made the decision to discontinue the study (one after the sildenafil assessment phase, the other after the tadalafil initiation phase), one patient discontinued because of a lack of efficacy, as perceived by the patient (after the tadalafil initiation phase), and another patient discontinued as a result of adverse events (headache, facial flushing and gastric discomfort; after the tadalafil initiation phase).

3.2 Patient treatment preference

Of the 156 patients expressing a treatment preference (as noted at Visit 5), 115 (73.7%) elected to take tadalafil during the 12-week extension phase, compared to 41 (26.3%) patients who elected to take sildenafil ($P < 0.001$). Baseline clinical and demographic patient characteristics by treatment preference group are outlined in Table 2.

3.3 PAIRS domain scores

PAIRS domain scores, analyzed using linear mixed effects models adjusting for baseline score (Visit 2), are summarized in Figure 2 (time concern), Figure 3 (sexual spontaneity) and Figure 4 (sexual self-confidence). After switching from sildenafil to tadalafil, a statistically significant ($P = 0.002$) decrease in the mean PAIRS time concern domain scores was observed,

Table 2. Baseline and treatment preference clinical and demographic characteristics. †Four patients discontinued prior to the extension phase (one after the sildenafil assessment phase and three after the tadalafil initiation phase); ‡Percentage does not sum to 100 because of rounding; §According to each investigator's clinical judgment. ED, erectile dysfunction; SD, standard deviation.

Characteristic	Total (n = 160)	Tadalafil preference (n = 115)†	Sildenafil preference (n = 41)†
Mean age (year ± SD [range])	55.0 ± 8.9 (32–75)	55.0 ± 9.1 (32–75)	55.6 ± 8.5 (34–71)
Mean weight (kg ± SD)	69.3 ± 8.6	69.4 ± 8.6	68.8 ± 7.9
Race/ethnicity (%)			
East/Southeast Asian	160 (100)	115 (100)	41 (100)
ED etiology (%)‡,§			
Psychogenic	11 (6.9)	8 (7.0)	1 (2.4)
Organic	82 (51.3)	61 (53.0)	19 (46.3)
Mixed	67 (41.9)	46 (40.0)	21 (51.2)
ED severity (%)‡,§			
Mild	32 (20.0)	19 (16.5)	13 (31.7)
Moderate	110 (68.8)	82 (71.3)	24 (58.5)
Severe	18 (11.3)	14 (12.2)	4 (9.8)
ED duration (%)‡			
< 1 year	18 (11.3)	13 (11.3)	4 (9.8)
> 1 year	142 (88.8)	102 (88.7)	37 (90.2)
Mean prior sildenafil use (days ± SD)	737 ± 574	711 ± 569	841 ± 601
Median prior sildenafil use (days [range])	585 (43–2 016)	530 (43–1 924)	640 (49–2 016)
Sildenafil entry dose (mg, %)			
50	73 (45.6)	59 (51.3)	12 (29.3)
100	87 (54.4)	56 (48.7)	29 (70.7)
Current alcohol use (%)	101 (63.1)	73 (63.5)	25 (61.0)
Current smoker (%)	43 (26.9)	32 (27.8)	10 (24.4)

with a mean (± SD) PAIRS time concern domain score of 2.54 (± 0.34) at Visit 3 (after the sildenafil assessment phase) and 2.42 (± 0.38) at Visit 5 (after the tadalafil assessment phase; Figure 2). No statistically significant differences were observed, after switching from sildenafil to tadalafil, in the mean PAIRS spontaneity and self-confidence domain scores (Figures 3 and 4).

3.4 Change in PAIRS domain scores based on preference

The change in PAIRS domain scores, based on patient treatment preference groups, between the sildenafil (Visit 3) and tadalafil (Visit 5) assessment phases, was determined using an analysis of covariance model with terms for patient's treatment preference and baseline PAIRS score. A reduction in time concerns was observed regardless of the patient's treatment preference; however, these reductions were not significantly different between preference groups (P = 0.70; mean change [± SD]: –0.12 [± 0.37] in patients preferring sildenafil, –0.11 [± 0.39] in patients preferring tadalafil). Likewise, no statistically significant changes in spontaneity were observed, in either preference group, between the sildenafil and tadalafil assessment phases (P = 0.33; mean change [± SD]: –0.02 [± 0.48] in patients preferring sildenafil, 0.03 [± 0.30] in patients preferring tadalafil). Significantly different changes in sexual self-confidence were, however, observed between preference groups (P = 0.011), with improvements in sexual self-confidence observed in patients preferring tadalafil (mean change [± SD]: 0.12 [± 0.42]), while a decrease in sexual self-confidence was observed in patients preferring sildenafil (mean change [± SD]: –0.08 [± 0.49]).

3.5 Dosing and sexual attempt timing

A statistically significant (P < 0.001) difference in

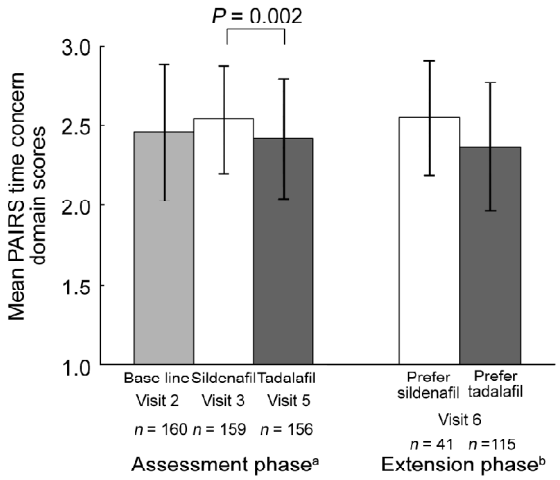

Figure 2. Mean Psychological and Interpersonal Relationship Scales (PAIRS) time concern domain scores. [a]PAIRS time concern domain scores were obtained at Visit 2 (prior to the sildenafil assessment phase), Visit 3 (after the sildenafil assessment phase, 4 weeks) and Visit 5 (after the tadalafil assessment phase, 4 weeks). [b]At Visit 5 patients were given the opportunity to choose either sildenafil or tadalafil for treatment during the extension phase (12 weeks), with PAIRS time concern domain scores being obtained at Visit 6 (on completion of the study, after the extension phase) based on the patient preferences.

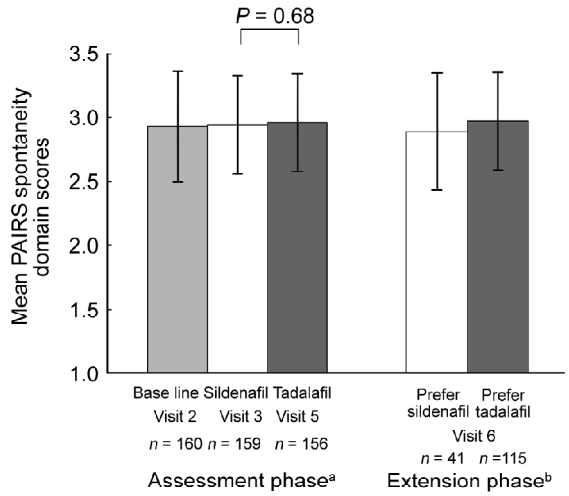

Figure 3. Mean Psychological and Interpersonal Relationship Scales (PAIRS) spontaneity domain scores. [a]PAIRS Spontaneity Domain Scores were obtained at Visit 2 (prior to the sildenafil assessment phase), Visit 3 (after the sildenafil assessment phase, 4 weeks) and Visit 5 (after the tadalafil assessment phase, four 4 weeks). [b]At Visit 5 patients were given the opportunity to choose either sildenafil or tadalafil for treatment during the extension phase (12 weeks), with PAIRS spontaneity domain scores being obtained at Visit 6 (on completion of the study, after the extension phase) based on the patient preferences.

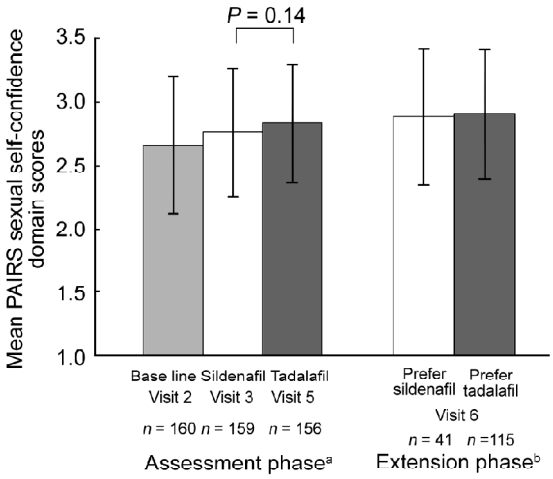

Figure 4. Mean Psychological and Interpersonal Relationship Scales (PAIRS) sexual self-confidence domain scores. [a]PAIRS sexual self-confidence domain scores were obtained at Visit 2 (prior to the sildenafil assessment phase), Visit 3 (after the sildenafil assessment phase, 4 weeks) and Visit 5 (after the tadalafil assessment phase, 4 weeks). [b]At Visit 5 patients were given the opportunity to choose either sildenafil or tadalafil for treatment during the extension phase (12 weeks), with PAIRS sexual self-confidence domain scores being obtained at Visit 6 (on completion of the study, after the extension phase) based on the patient preferences.

median time from dose to sexual attempt was observed between the sildenafil and tadalafil assessment phases, with a median time between dosing and sexual attempt of 1 h (ranging from 0 h to 6 h) during the sildenafil assessment phase and 1.5 h (ranging from 0 h to 15 h) during the tadalafil assessment phase.

Differences in the proportion of sexual attempts, occurring over a 36-h timeframe, were observed between the sildenafil and tadalafil assessment phases. During the sildenafil assessment phase patients reported 4.5% of sexual attempts occurred > 4 to ≤ 36 h post-dose, whereas this proportion increased to 17.5% during the tadalafil assessment phase.

3.6 Tolerability

There were no deaths or serious adverse events reported during the present study; however, one patient discontinued, after the tadalafil initiation phase, because of several adverse events (headache, facial flushing and gastric discomfort). Treatment-emergent adverse events were reported in 13.1% (sildenafil assessment phase), 13.8% (tadalafil initiation phase), and 12.2% (tadalafil assessment phase) of patients. The most frequently oc-

curring (≥ 1%) treatment-emergent adverse events reported during the sildenafil assessment phase were flushing (n = 10, 6.3%), nasal congestion (n = 3, 1.9%) and headache (n = 2, 1.3%); during the tadalafil initiation phase were flushing (n = 3, 1.9%), epigastric discomfort (n = 3, 1.9%), headache (n = 3, 1.9%), hypertension (n = 3, 1.9%) and nasopharyngitis (n = 2, 1.3%); and during the tadalafil assessment phase were headache (n = 2, 1.3%) and hypertension (n = 2, 1.3%).

4 Discussion

Because there are several effective and safe oral PDE-5 inhibitors (sildenafil citrate, vardenafil hydrochloride and tadalafil) for the treatment of ED, various factors (such as biological, social, psychological and/or cultural) important to both the patient and their partner will influence the treatment choices made. Although several previous studies have focused on determining patient treatment choices [8–10], the reasons surrounding these treatment choices have not been fully explored. The present study was conducted primarily to evaluate patient preferences for sildenafil or tadalafil in the treatment of ED, and the potential reasons for these preferences, within a cohort of current sildenafil users in Korea. The majority of patients expressing a treatment preference elected to take tadalafil (73.7%) during the 12-week extension phase, whereas the remainder (26.3%) chose to take sildenafil. This finding is in alignment with several previous studies, where the majority of patients expressed a treatment preference for tadalafil, as opposed to sildenafil [8–10].

PAIRS were developed to incorporate outcomes, such as time concerns, spontaneity and sexual self-confidence, which are not assessed in existing measures of sexual function. This is another approach that can be used to identify some of the possible reasons as to why patients have preferences for one form of treatment over another. A statistically significant decrease in the mean PAIRS time concern domain scores was observed when patients switched from sildenafil (Visit 3) to tadalafil (Visit 5), indicating that patients were less concerned about time in relation to sexual activity whilst taking tadalafil, as compared with when they were taking sildenafil. A study by Rosen *et al.* [11] showed similar results to those in the present study, whereby mean PAIRS time concern domain scores were statistically significantly lower after treatment with tadalafil when compared to post sildenafil treatment. In the present study, mean PAIRS time concern domain scores in those choosing sildenafil in the extension phase were also numerically higher (i.e. worse) than those who chose tadalafil. Furthermore, regardless of treatment preference, similar reductions in time concern domain scores, from the sildenafil to tadalafil assessment phase, were observed. Together, these results suggest that time concerns appear to play a role in patient decisions regarding ED treatment type.

No statistically significant difference in the mean PAIRS spontaneity domain scores was observed in the present study when patients switched from sildenafil (Visit 3) to tadalafil (Visit 5). Furthermore, there was no difference in mean PAIRS spontaneity domain scores in patients choosing to take sildenafil or tadalafil in the extension phase. It is of interest to note that previous studies, encompassing patients in Australia, Canada, Italy, Sweden, the UK and the USA, report statistically significantly higher sexual spontaneity in patients on tadalafil treatment when compared with sildenafil treatment [11, 12]. Also, studies in Asian populations, such as Hong Kong (China), Malaysia, Singapore, Taiwan (China) and the Philippines, have shown statistically significant differences between the two treatment groups in all three PAIRS domains [13, 14]. We are not sure why we did not observe this finding in the current study, but it is possible that this Korean population or the Korean culture does not place great importance on sexual spontaneity.

Although Rosen *et al.* [11] observed higher sexual self-confidence in patients taking tadalafil than that in patients taking sildenafil, in the present study no statistically significant difference in the mean PAIRS self-confidence domain scores was observed when patients switched from sildenafil (Visit 3) to tadalafil (Visit 5). Again, our finding could be attributed to cultural differences. However, statistically significant differences between the two treatment groups in PAIRS self-confidence domain scores have been observed in similar geographical locations (Hong Kong [China], Malaysia, Singapore, Taiwan [China] and the Philippines) [13, 14]. Additionally, there was no difference in mean PAIRS self-confidence domain scores in patients choosing to take sildenafil or tadalafil in the extension phase. However, statistically significant differences between the two preference groups were observed in terms of change in sexual self-confidence (from Visit 3 to Visit 5), with improvements in self-confidence observed in

patients preferring tadalafil, wheras those preferring sildenafil showed decreased sexual self-confidence. These findings suggest that sexual self-confidence might be a consideration when patients make a choice regarding treatment for ED.

Another factor that might play a role in the decision a patient makes regarding the choice of PDE-5 inhibitor is the window of opportunity available to them for sexual activity post-dose. Timing of dose to sexual attempt patterns were assessed in each treatment group to determine whether experienced sildenafil patients changed their behavior with new dosing instructions, for tadalafil, to suggest a broader window of opportunity from dose to sexual intercourse. Although a statistically significant increase in median time from dose to sexual attempt was observed during the tadalafil assessment phase, when compared with the sildenafil assessment phase, this increase was not of clinical relevance and could be a result of the treatment specific dosing instructions. This indicates that, on average, previous sildenafil users in the present study did not modify their sexual attempt timing greatly even when provided with a treatment option that allowed for increased time from dose to sexual attempt. Interestingly, in previous studies, a statistically and clinically significant difference has been observed between the two treatment groups in terms of time from dose to sexual attempt, with greater time from dose to sexual attempt being observed in tadalafil treated patients [9, 10, 15]. It is possible that cultural differences play a role in the extent to which patients experiment beyond their normal dose-timing patterns. Previous studies have shown that the magnitude of change observed in dose-timing patterns, when patients change from sildenafil to tadalafil, varies between different geographical locations, with smaller changes in dose-timing patterns observed in Asian countries [13, 16] when compared to central/eastern Europe and eastern Mediterranean regions [17], and Australia and New Zealand [18]. Although the median time from dose to sexual attempt did not differ clinically between the two treatment groups, the window of time in which sexual attempts were being made was broader during the tadalafil assessment phase when compared to the sildenafil assessment phase. Previous studies [10, 15] also show that sexual attempts are made over a broader time period when patients are taking tadalafil, when compared to sildenafil. It is possible that the larger window of opportunity observed in the present study during the tadalafil assessment phase might be a result of the different dosing instructions, as for the two treatment types, as patients were informed that tadalafil had been shown to be effective up to 24 h post-dose, whereas sildenafil could be taken up to 4 h before sexual activity. Additionally, with tadalafil, patients were advised to initiate sexual activity at various times after dosing to determine their own optimal window of responsiveness.

Although over 70% of patients in the present study expressed a preference for tadalafil during the extension phase, it is somewhat surprising that PAIRS time concern domain scores were the only measure in which statistically significant differences between the two groups support this preference pattern. One possible explanation for this disparity might be that there are other factors, not analyzed in the current study, that might be responsible for the patient preference patterns observed [19]. Furthermore, although the present study measured the number of sexual attempts made by patients during each treatment phase, the number of successful sexual attempts was not measured and it is possible that the incorporation of other measures, such as efficacy measures (International Index of Erectile Function [IIEF] or Sexual Encounter Profile [SEP]), or a drug attribute questionnaire, might have furthered our understanding of why patients exhibit particular preferences for treatments. Additionally, it is possible that differences in spontaneity and sexual self-confidence might not have been experienced by the patients as they did not appear to utilize the extended period of efficacy offered by tadalafil.

The present study indicates that both sildenafil and tadalafil are well-tolerated, as reflected by other studies [9, 10, 15]. The frequency and type of treatment-emergent adverse events (TEAE) reported in the present study were similar between the two treatment groups, and it therefore seems unlikely that TEAE were a factor in patient preference choices.

There are several limitations of the present study that should be taken into account when interpreting its results. First, sildenafil-specific and tadalafil-specific dosing instructions were given consistent with product labeling. Although bias is incurred as a result, the open-label nature of the design was chosen to ensure that instructions would be therapy-specific. Additionally, as patients had previous experience with sildenafil it would be likely, even if blinding occurred, that patients would be able to determine the treatments due to the differences in dosing instructions. Second, patients

received treatment in a fixed order (sildenafil followed by tadalafil) and it is possible that patients might have preferred whichever treatment they received last. As patients had been previous long-term sildenafil users, we believe that because of the short amount of time in which patients were taking tadalafil during the assessment phase, the likelihood of patients continuing with tadalafil if they did not actually prefer the new treatment would have been relatively low. Further to this, other studies have shown that the sequence in which treatments are given (i.e. sildenafil followed by tadalafil or vice versa) does not appear to affect patient treatment preference [10, 20]. Third, although the issue of imbalance between groups was attempted to be addressed by adjusting for baseline confounders, it is possible that these baseline corrections might not fully address the potential biases of this open-label study. Finally, interest in a novel therapy might have increased the proportion of patients electing to take tadalafil during the extension phase, when compared with sildenafil.

Although the current study focuses purely on patients within Korea, this may be viewed as a strength as it provides ED information on a distinct cultural group, especially in light of the fact that the PAIRS findings for this study seem to be contradictory to what has been observed for other populations. The median duration of previous sildenafil use might be considered a strength of the present study, as optimal efficacy and tolerability of sildenafil should have been established prior to the assessment phase.

This study not only focuses on patient treatment preferences, but also attempts to identify the reasons surrounding a patients' choice of treatment for ED, as increased knowledge of the factors contributing to patient treatment choices will enable physicians to determine the most appropriate treatment for their patients. The present study shows that after patients had experienced both sildenafil and tadalafil, the majority of patients exhibited a preference for tadalafil. The results also suggest that this preference for tadalafil might be influenced in part by psychosocial factors and the window of opportunity available for sexual activity, as a decrease in time concerns was observed during the tadalafil assessment phase and the window of time in which sexual attempts were being made was broader during the tadalafil assessment phase. Furthermore, the results also suggest that the importance of different factors might vary as a result of different cultural groups.

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