Efficacy and Safety of Sildenafil in Asian Males with Erectile Dysfunction and Cardiovascular Risk

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Objective: *Assess the effectiveness of sildenafil in Asian males with erectile dysfunction (ED) and one or more of the co-morbidities, mild-to-moderate hypertension, dyslipidemia, and diabetes.*
Material and Method: *A six-week, double-blind, randomized, placebo-controlled, multicenter study was carried out in Thailand, Malaysia and Singapore One hundred and fifty five male subjects were randomized (2:1) to sildenafil (n = 104) or placebo (n = 51). Sildenafil was started at 50mg and increased (100 mg) or decreased (25mg) at week 2 if necessary.*
Results: *On the primary efficacy endpoint, sildenafil-treated subjects had significantly better scores on the International Index of Erectile Function (IIEF) questions 3 and 4 than placebo ($p < 0.001$, both questions). When accumulated into IIEF domains, all five domains were significant in favor of sildenafil. In addition, sildenafil-treated subjects were more satisfied with treatment and had a higher intercourse success rate. The majority of adverse events were mild in severity; the most commonly reported treatment-related events were dizziness (7.7%) and tinnitus (2.9%).*
Conclusion: *Sildenafil (25, 50, and 100 mg) was found to be an effective, safe, and well-tolerated treatment for ED in the present study population of Thai, Malaysian, and Singaporean males who also had increased cardiovascular risk*

Keywords: *Sildenafil, Erectile dysfunction, Randomized controlled trial,Cardiovascular risk, Diabetes mellitus*

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Erectile dysfunction (ED) has been reported to affect over 150 million men globally due to various etiologies[1]. Studies of men above the age of 40 in Thailand, Malaysia, and Singapore have reported a prevalence of ED as 38%, 60%, and 59%, respectively[2-4]. Erections are achieved as a result of a series of cascading pathways that include psychological, neurological, endocrine, vascular, and muscular factors. Therefore, problems with any one of these individual systems could trigger ED[2]. Consequently, ED is

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categorized into three domains: organic, mixed, and/or psychogenic - with organic-based causes being the most predominant[5,6].

Diabetes, hypertension, dyslipidemia, cigarette smoking, obesity, and sedentary lifestyles are highly prevalent in men with ED[7-16]. Moreover, the severity of ED increased in men with cardiovascular disorders and type II diabetes mellitus. The link between hypertension and ED stems from the significant long-term damage hypertension can cause in the vascular system and tissues. Chronic hypertension has a drastic affect on the miniscule network of penile blood vessels, which is the focal pathway for erection[17]. In patients with diabetes, 35 to 75% suffer from some degree of ED since diabetes can compromise erectile responses via all four mechanisms (vascular, neural, local-tissue, and endocrine)[6,8,18,19]. Diabetes is responsible for a 3 to 4-fold increase in the risk of ED, particularly in men with neuropathy, severe depressive symptoms, and/or current or former nicotine use[20].

Despite a range of effective ED therapies such as vacuum constriction devices, penile implants, vasoactive injection therapy, transurethral alprostadil therapy, and oral therapies, 70-90% of men with ED do not choose to seek treatment[6,21-24]. Men who receive treatment generally choose oral phosphodiesterase type 5 (PDE5) inhibitor therapies such as sildenafil (Viagra)[5]. Although sildenafil was initially indicated for angina pectoris, it was the first oral PDE5 inhibitor approved for treatment of ED. The PDE5 enzyme is the sole component responsible for degradation and inactivation of cyclic guanosine monophosphate (cGMP), which results in termination of an erection. Sildenafil selectively inhibits PDE5 and thereby contributes to the induction and/or persistence of an erection. Favorably, sildenafil only acts when an individual has had sufficient sexual arousal to promote an erection[6]. While hypertension is a risk factor for ED, many antihypertensive agents may worsen sexual function as a drug specific side effect. The PDE5 inhibitors are well tolerated when given in combination with antihypertensives to patients with hypertension, provided baseline blood pressure is at least 90/60 mmHg; however, PDE5 inhibitors are contraindicated with nitric oxide donors and alpha adrenoceptor blockers.

The efficacy of sildenafil has been evaluated in multiple studies of males with ED of various etiologies. At doses of 25, 50, or 100 mg in 21 randomized, double-blind placebo-controlled trials, 3000 subjects taking sildenafil experienced statistically significant improvements. In fixed dose studies, the number of subjects reporting improved erections was 63% (25 mg) from treatment 74% (50 mg), and 82% (100 mg) with sildenafil compared with 24% on placebo[25]. Long-term studies of up to 4 years have also been conducted on the efficacy of sildenafil[26-28]. McMurray et al, found that satisfaction with treatment was 98.1%, 96.6%, 94.8%, and 96.3% at the end of years 1, 2, 3, and 4, respectively. Additionally, improvement in the ability to engage in sexual activity was reported in 99.6%, 99.9%, 99.8%, and 100% of subjects at the end of each year[26].

Studies have shown that sildenafil is a well-tolerated and safe treatment for ED[25]. Commonly reported adverse events from studies totaling 4274 subjects 18-87 years of age who received double-blind treatment for ED were headaches (16%), flushing (10%), and dyspepsia (7%). Adverse events were predominantly transient and mild or moderate in nature[27].

Although it is well known that hypertension, dyslipidemia, and diabetes are risk factors for ED, no studies have evaluated the efficacy and safety of sildenafil for treatment of ED in Asian males who also have these co-morbidities, and hence have increased cardiovascular risk. Accordingly, the present study was designed to assess the efficacy and safety of sildenafil, administered as required, to Asian males with ED and one or more of the following co-morbidities: mild-to-moderate arterial hypertension, dyslipidemia, and/or type II diabetes mellitus.

Material and Method

The present study was carried out from May 2001 to February 2003 at eight study centers in Thailand (5), Malaysia (2), and Singapore (1). The present study was conducted in accordance with the ethical principals outlined in the Declaration of Helsinki, and in compliance with the International Conference on Harmonization Good Clinical Practice guidelines and local regulatory requirements. The protocol (study code: A1481034) was approved by the Institutional Review Board at each centre and written informed consent was obtained from each subject as a condition of entry.

Study Design

This was a six-week, double blind, randomized, placebo-controlled, multicenter study. There were four study visits: screening (week -2), baseline (week 0), and evaluation visits at weeks 2 and 6 (final visit). At baseline event logs, which were distributed at screening, were reviewed for appropriate completion

and eligible subjects were randomized (2:1) to treatment or placebo using a computer-generated randomization schedule provided by the sponsor prior to the present study. All subjects were started on 50 mg sildenafil (or equivalent placebo). If necessary, this dose was increased to 100 mg or decreased to 25 mg at week 2 based on the investigators opinion of efficacy, safety, and tolerability. Subjects were only allowed to take one dose of study medication per day, which was taken one hour prior to the anticipated sexual activity.

Inclusion Criteria

The present study included male subjects with a documented history of ED (> six months) who were at least 21 years old with one or more of the co-morbidities, mild-to-moderate arterial hypertension, dyslipidemia, and type II diabetes mellitus. Study specific co-morbidities were required to be stable for at least six months prior to screening. Erectile dysfunction was clinically diagnosed, documented, and confirmed by a modified Sexual Health Inventory for Men (SHIM), International Index of Erectile Function (IIEF-5) score ≤ 21 at screening and a total erectile function domain score (items 1-5 and 15 of the IIEF) ≤ 25 at baseline. In addition, subjects were required to be in a stable heterosexual relationship for at least six months with the opportunity for regular sexual intercourse.

Any of the following rendered a subject ineligible, prescribed and/or taking nitrates or nitric oxide, hormonal replacement therapy or ritonavir, known intolerance or sensitivity to sildenafil, hormonal or sexual disorders, genital anatomical deformities that would impair erection, recent cardiovascular disease, severe renal dysfunction or severe hepatic disease, degenerative retinal conditions, psychiatric disorders, history of hematological abnormalities, or known history of alcohol or substance dependence within the previous two years. In addition, subjects with poorly controlled study specific co-morbidities were excluded, hypertension (systolic blood pressure > 170 or < 90 mmHg and/or diastolic blood pressure > 110 or < 50 mmHg or orthostatic hypotension), dyslipidemia (total serum cholesterol > 240 mg/dL and/or total serum triglycerides > 400 mg/dL), diabetes (glycosylated hemoglobin > 10% and/or diabetic retinopathy).

Evaluations

The primary endpoints were the responses to questions 3 and 4 on the IIEF, which address a subject's ability to achieve successful intercourse. Secondary endpoints included the responses to the remaining IIEF questions (1, 2, 5-15), the IIEF domain scores i.e., erectile function domain (sum of question 1-5 and 15), orgasmic function domain (sum of question 9 and 10), sexual desire domain (sum of question 11 and 12), intercourse satisfaction domain (sum of question 6-8), and overall satisfaction domain (sum of question 13 and 14), the responses to the Global Efficacy Assessment Questions, the intercourse success rate derived from the subject event log, and the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS). Efficacy measures were assessed at baseline and end of treatment (week 6) or at the time of discontinuation if a subject prematurely discontinued. Safety evaluations included a physical examination at screening and final visit, vital signs and adverse events were monitored at every visit, and routine laboratory measurements were taken at screening and at any point throughout the study if necessary.

Statistical Analysis

There were three populations analyzed: 1) the safety population included all subjects who took at least one dose of study medication, 2) the intent-to-treat (ITT) population included all subjects in the safety population who provided at least one post-baseline efficacy assessment, and 3) the evaluable (EVAL) population included all subjects in the ITT population who adhered strictly to the protocol, were compliant with the study medication, and answered IIEF questions 3 and 4 at baseline and post baseline.

The primary efficacy endpoints (IIEF 3 and 4) were analyzed separately by a one sample t-test using the ITT and EVAL populations - both of which were required to be significant at the 5% level (two-sided) in order to claim efficacy. Secondary efficacy variables - IIEF 1, 2, 5-15, domain scores and EDITS - were analyzed using the same method used for the primary analyses using only the ITT population. The Global Efficacy Assessment Questions and the subject event logs were summarized using proportions and 95% confidence intervals (CI). Last observation carried forward (LOCF) methodology was used.

Result

Subject Disposition

One hundred and fifty five subjects were randomized to treatment (104 sildenafil; 51 placebo). Seven subjects (4.5%) prematurely discontinued six of whom discontinued from the sildenafil arm. Subject disposition is summarized in Fig. 1.

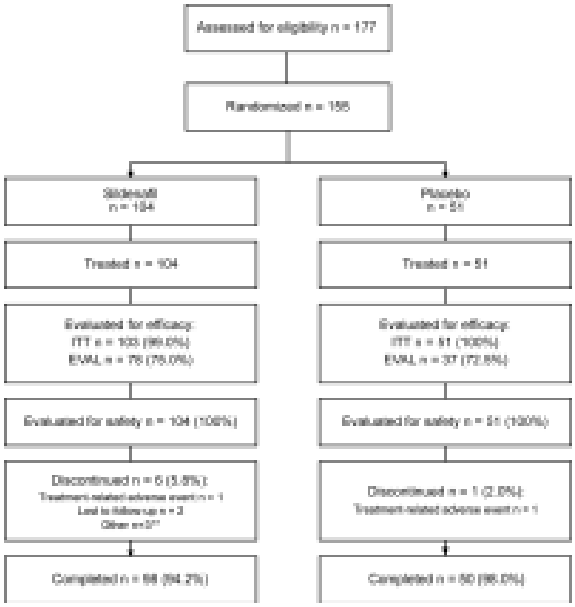

Fig. 1 Subject Disposition
ITT, intent-to-treat analysis population. EVAL, evaluable analysis population. * One subject did not have a post-baseline efficacy assessment. ** One subject was denied by their partner; one subject had a positive serology for syphilis; one subject absconded with study medication.

Demography and Baseline Characteristics

Demography and baseline characteristics are summarized in Table1. Treatment groups were well matched at baseline with the exception of the duration of diagnosis of ED - subjects in the placebo arm had a longer duration of diagnosis of ED spanning a longer period (range 0.2 to 29.0 years) compared with subjects in the sildenafil arm (range 0.1 to 10.0 years).

In terms of the distribution of study specific co-morbidities, as single risk factors hypertension and diabetes had a higher prevalence than dyslipidemia in both groups. Presence of two co-morbidities was frequent in both arms: a combination of hypertension and diabetes was predominant in the sildenafil group while a combination of hypertension and dyslipidemia was predominant in the placebo group. A relatively high proportion of subjects had all three concomitant conditions. Diabetes was diagnosed for slightly longer in the placebo group compared with sildenafil (8.6 $\pm$ 7.8 versus 6.7 $\pm$ 5.3 years); duration of diagnosis of hypertension (7.3 $\pm$ 7.1 sildenafil; 7.5 $\pm$ 5.7 placebo), and dyslipidemia (3.2 $\pm$ 2.5 sildenafil; 3.4 $\pm$ 3.2 placebo) was similar for both groups.

Antihypertensive drugs (52.9% sildenafil; 64.7% placebo), diabetic drugs (50.0% sildenafil; 51.0% placebo), beta-blockers (23.1% sildenafil; 33.3% placebo), and drugs for hyperlipidemia (23.1% sildenafil; 29.4% placebo) were the most frequently prescribed concomitant medications. Drugs used in rheumatic diseases and gout were also commonly used (21.2% sildenafil; 19.6% placebo).

Study Drug Administration

At visit 2, 51.9% (n = 54) of the subjects in the sildenafil group and 84.3% (n = 43) of subjects in the

Table 1. Demography and baseline characteristics

Measure	Sildenafil	Placebo
Safety Population	n = 104	n = 51
Mean age, years (SD)	55.4 (8.7)	55.7 (7.6)
Mean weight, kg (SD)	70.9 (12.7)	71.1 (10.9)
Mean height, cm (SD)	166.3 (6.2)	165.6 (6.0)
ITT Population	n = 103	n = 51
Duration of diagnosis of ED, years (SD)	2.5 (2.1)	4.4 (5.6)
Modified SHIM IIEF-5, mean (SD)	10.8 (4.5)	9.9 (5.4)
IIEF erectile function domain score, mean (SD)	14.3 (5.2)	13.1 (6.0)
Hypertension, n (%)	22 (21.4)	12 (23.5)
Type II diabetes, n (%)	20 (19.4)	9 (17.6)
Dyslipidemia, n (%)	3 (2.9)	1 (2.0)
Hypertension and type II diabetes, n (%)	22 (21.4)	7 (13.0)
Hypertension and dyslipidemia, n (%)	15 (14.6)	11 (21.6)
Type II diabetes and dyslipidemia, n (%)	9 (8.7)	3 (5.9)
Hypertension, type II diabetes and dyslipidemia, n (%)	12 (11.7)	8 (15.7)

SD, standard deviation. SHIM, Sexual Health Inventory for Men. IIEF-5, International Index of Erectile Function.

placebo had their dose increased to 100 mg; only one subject had his dose decreased to 25 mg as a result of a mild adverse event, this subject was in the sildenafil group. Overall, subjects in the sildenafil group took a greater number of doses of study medication compared with the placebo group: mean dose/week 3.5 $\pm$ 1.8 sildenafil versus 2.8 $\pm$ 1.6 placebo.

Efficacy

International index of erectile function (IIEF)

On the primary endpoint (IIEF questions 3 and 4) the responses at week 6 were significantly better with sildenafil treatment compared with placebo for the ITT analysis population ($p < 0.001$). The results for the EVAL analysis were similar and significant in favor of sildenafil, and thus confirming and supporting the findings from the ITT analysis (Table 2). Of the remaining 13 questions on the IIEF, 11 had significantly different and higher scores with sildenafil treatment compared with placebo. The only questions that were not significant were 6 ($p = 0.062$) and 12 ($p = 0.068$); question 6 rates intercourse frequency over the past 4 weeks, while question 12 rates level of desire over the past 4 weeks. When individual questions were accumulated into their respective domains, all five domains were found to be statistically significant in favor of sildenafil (Table 2).

Subject event logs

There was an increased number of attempts at sexual intercourse by subjects in the sildenafil group compared with placebo (1983 versus 776, respectively), as well as a higher number of successful attempts at sexual intercourse (1340 versus 283, respectively). Overall, subjects in the sildenafil group had 2.2 successful events per week (95% CI 2.1 to 2.3) compared with 0.9 (95% CI 0.8 to 1.0) in the placebo group.

Global efficacy assessment questions

On the Global Efficacy Assessment Questions, 86.4% (n = 89) of sildenafil-treated subjects reported that treatment improved erections compared with 43.1% (n = 22) in the placebo group. Similarly, 86.4% (n = 89) of the sildenafil-treated subjects answered that

Table 2. International index of erectile function (IIEF)

Parameter	Group	Baseline		Week 6/LOCF		p-value
		N	Mean (SD)	N	Mean (SD)	
Primary Endpoints (EVAL)						
IIEF Q3	Sildenafil	78	2.5 (1.2)		4.1 (1.2)	0.003
	Placebo	37	2.5 (1.4)		3.3 (1.4)	
IIEF Q4	Sildenafil	78	2.3 (1.3)		3.9 (1.4)	0.002
	Placebo	37	2.1 (1.2)		3.0 (1.4)	
Primary Endpoints (ITT)						
IIEF Q3	Sildenafil	103	2.5 (1.3)	101	4.0 (1.2)	<0.001
	Placebo	51	2.4 (1.4)	50	3.0 (1.4)	
IIEF Q4	Sildenafil	103	2.3 (1.2)	101	3.9 (1.4)	<0.001
	Placebo	51	2.0 (1.1)	50	2.8 (1.4)	
Secondary IIEF Accumulated Domains (ITT)						
Erectile function (Q1-5, 15)	Sildenafil	102	14.3 (5.2)	101	23.1 (6.7)	<0.001
	Placebo	51	13.1 (6.0)	50	17.7 (6.9)	
Orgasmic function (Q9 and 10)	Sildenafil	103	5.3 (2.7)	101	7.8 (2.4)	0.008
	Placebo	51	5.1 (3.0)	50	6.5 (2.9)	
Sexual desire (Q11 and 12)	Sildenafil	103	5.6 (1.8)	101	7.0 (1.6)	0.029
	Placebo	51	5.5 (1.7)	50	6.4 (1.9)	
Intercourse satisfaction (Q6-8)	Sildenafil	103	5.9 (2.4)	101	11.0 (2.9)	<0.001
	Placebo	51	5.6 (2.9)	50	8.5 (3.2)	
Overall satisfaction (Q13 and 14)	Sildenafil	103	4.7 (2.0)	101	7.7 (2.2)	<0.001
	Placebo	51	4.7 (2.1)	50	5.9 (2.4)	

IIEF, International Index of Erectile Function. SD, standard deviation. EVAL, evaluable analysis population. ITT, intent-to-treat analysis population. Q, question.

treatment improved their ability to have sexual intercourse compared with 39.2% (n = 20) in the placebo group.

Erectile dysfunction inventory of treatment satisfaction (EDITS)

The significantly higher EDITS mean score for the sildenafil group (72.9 ± 19.9) compared with the placebo group (53.5 ± 22.9) indicated that subjects taking sildenafil were generally more satisfied with their treatment and their intimate lives ($p < 0.001$).

Safety

In total, 26 (16.8%) subjects reported 42 individual treatment emergent adverse events (all causalities): 16 subjects (15.4%) in the sildenafil group had 31 adverse events; 10 (19.6%) subjects in the placebo group had 11 adverse events. The most commonly reported adverse events were dizziness (n = 9, 5.8%), respiratory tract infections (n = 5, 3.2%) and headaches (n = 5, 3.2%).

Twenty-three of the 42 treatment emergent adverse events were considered related to treatment and reported for 15 subjects (n = 10 subjects sildenafil). There were no serious adverse events recorded during the present study. Only one treatment-related adverse event, hypertension (placebo group), was considered severe. There were two adverse events that were moderate in severity, palpitations, and dizziness, both reported in the sildenafil group. All other treatment-related adverse events were mild in severity. Table 3 shows the incidence of treatment-related adverse events.

Table 3. Incidence of treatment-emergent treatment-related adverse events

Event	Sildenafil, n = 104		Placebo, n = 51	
	N	%	N	%
Dizziness	8	7.7	-	-
Tinnitus	3	2.9	-	-
Headache	2	1.9	1	2.0
Hot Flushes	2	1.9	1	2.0
Vasodilation	2	1.9	1	2.0
Hypertension	-	-	1*	2.0
Palpitation	1*	1.0	-	-
Chest Pain	-	-	1	2.0

Note: the following adverse events were reported multiple times by the same subject: vasodilation (x2), tinnitus (x3) and dizziness (2 times by 3 subjects each). * Subjects discontinued as a result of the event.

Of the seven (4.5%) subjects who discontinued from the present study, two discontinued as a result of treatment-related adverse events - one subject discontinued from the sildenafil group as a result of moderate palpitations; one subject discontinued from the placebo group as a result of severe hypertension. All other discontinuations were unrelated to study medication.

Discussion

Overall, sildenafil (25, 50 and 100 mg) was found to be a highly efficacious, safe and well-tolerated treatment for ED in this Asian study population who also had one or more of the co-morbidities mild-to-moderate arterial hypertension, dyslipidemia and type II diabetes mellitus. Indeed, the efficacy profile of sildenafil observed in the present study correlates well with results from other Western and Asian studies that have previously demonstrated the effectiveness of sildenafil when administered in 25, 50 or 100 mg doses[2,5,25,29,30].

On the primary efficacy result (IIEF questions 3 and 4), sildenafil was found to be significantly more effective than placebo (note: as the findings were significant for both primary endpoint IIEF questions, efficacy can be claimed). These findings are mirrored in many Asian[2,5,30] and Western studies[25,31-34] some of which also contained study populations with subjects who had concomitant cardiovascular disorders or diabetes. In the present study, the presence of one or more of the study specific co morbidities (hypertension, dyslipidemia and diabetes) did not compromise the effectiveness of sildenafil; a finding that has been observed in other studies where subjects with co-morbidities (such as diabetes, ischemic heart disease, peripheral vascular disease or hypertension) also experienced significant results on ED efficacy parameters[5,29,35]. Although some Western studies have observed a slightly suppressed efficacy with sildenafil in subjects with diabetes, comparisons with placebo still showed marked differences in the improvement of erectile function[5,34,36-38]. In addition, it has previously been shown that men with ED and concomitant hypertension who have taken sildenafil have an improved erectile function domain score, along with IIEF questions 3 and 4, when compared with placebo[39]. It has also been shown that sildenafil-treated subjects with ED and hypertension are also more likely to have improved erections, improved number of attempts and a

higher number of successful attempts compared with placebo despite the fact that both hypertension and antihypertensive agents can contribute to (or cause) ED and to the severity of ED[5].

The secondary efficacy results reaffirm the strength of sildenafil in the present study population. The Global Efficacy Assessment Questions, EDITS, IIEF (secondary endpoint questions), and the subject logs all demonstrated significant differences between the sildenafil and placebo groups thus reinforcing the overall efficacy of sildenafil in different respects. Only two IIEF questions (6 and 12) had non-significant differences between the groups. However, the summation of their respective domains (intercourse satisfaction and sexual desire) still equated to a notable difference. The number of subjects reporting successful attempts at intercourse, improved ability to have sexual intercourse or overall satisfaction, was higher in the sildenafil group. The significant findings on the secondary endpoints in the present study have also been observed in two other Asian studies, which consisted of a Thai population[2] and a Malaysian, Singaporean and Filipino population[30].

The safety profile of sildenafil in the present study resembles that of other studies[2,29,32,34]. The severity of treatment-related adverse events in the present study was primarily mild, with two moderate cases and only one severe case. Discontinuations as a result of adverse events were low (1.3%) in the present study compared with other studies (3.0%)[31,32]. The most frequently occurring treatment emergent, treatment-related adverse events had a very low incidence and included dizziness (7.7%) tinnitus (2.9%), headaches (1.9%), hot flushes (1.9%), and vasodilation (1.9%); these types of events were expected based on previous reports on the safety profile of sildenafil[27]. Notably, there were no serious adverse events reported for subjects in the present study, while other studies have observed an average incidence of serious adverse event cases of 2.5%[31,32].

Conclusion

Sildenafil (25, 50, and 100 mg) was found to be an effective, safe, and well-tolerated treatment for ED in the present study population of Thai, Malaysian, and Singaporean males who also had increased cardiovascular risk. Notwithstanding the presence of risk factors for ED (hypertension, dyslipidemia, and diabetes) in the present study population, the effectiveness of sildenafil was significantly improved compared with placebo and comparable to studies in populations without increased ED risk factors present.

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การศึกษาประสิทธิผลและความปลอดภัยของยา ซิลเดนาฟิล ในชายเอเชียที่มีอาการหย่อนสมรรถภาพทางเพศและมีความเสี่ยงของโรคหลอดเลือดหัวใจ

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การศึกษาวิจัยแบบสุ่มปิดการรักษาทั้งสองทาง ที่มียาไม่ออกฤทธิ์เป็นตัวควบคุม แบบคู่ขนาน สหสถาบันในประเทศไทย มาเลเซีย และ สิงคโปร์ เพื่อประเมินประสิทธิผลของยา ซิลเดนาฟิล ในชายชาวเอเชียที่มีอาการหย่อนสมรรถภาพทางเพศและมีโรคต่อไปนี้ร่วมด้วย หนึ่ง หรือ สอง ชนิด คือโรคความดันโลหิตสูงระดับเล็กน้อยถึงปานกลาง ภาวะไขมันในเลือดผิดปกติ และ เบาหวาน อาสาสมัครชายรวมทั้งสิ้นจำนวน 155 รายได้รับการสุ่ม (2:1) เพื่อรับยาซิลเดนาฟิล (104 ราย) หรือยาไม่ออกฤทธิ์ (51 ราย) โดยยาซิลเดนาฟิลมีขนาดเริ่มต้นที่ 50 มิลลิกรัม ถ้ามีความจำเป็นอาจจะมีการปรับขนาดยาเพิ่มขึ้นเป็น 100 มิลลิกรัม หรือลดลงเป็น 25 มิลลิกรัมในสัปดาห์ที่ 2 การประเมินประสิทธิผลหลักโดยใช้แบบสอบถามสมรรถภาพทางเพศชาย (IIEF) ข้อ 3 และ 4 พบว่าอาสาสมัครในกลุ่มที่ได้รับยาซิลเดนาฟิลมีประสิทธิผลดีกว่าอาสาสมัครในกลุ่มที่ได้รับยาไม่ออกฤทธิ์อย่างมีนัยสำคัญทางสถิติ ($p < 0.001$) และเมื่อประเมินผลจากคะแนนรวมของสมรรถภาพแต่ละด้าน (IIEF domains) พบว่ายาซิลเดนาฟิลยังคงมีประสิทธิผลดีอย่างมีนัยสำคัญ นอกจากนี้ยังพบว่าอาสาสมัครที่ได้รับยาซิลเดนาฟิลมีความพึงพอใจในการรักษาและประสบความสำเร็จในการมีเพศสัมพันธ์สูง อาการไม่พึงประสงค์ที่พบส่วนใหญ่มีความรุนแรงระดับเล็กน้อย อาการไม่พึงประสงค์ที่พบบ่อยและมีความสัมพันธ์กับการรักษาคืออาการมึนศีรษะ (7.7%) และหูอื้อ (2.9%)