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REVIEW

Prevalence and medical management of erectile dysfunction in Asia

Kwangsung Park, Eu Chang Hwang and Sun-Ouck Kim

Erectile dysfunction (ED) is an important worldwide health issue that has a significant negative impact on the quality of life and life satisfaction of both the affected individual and his partner. Here we review the prevalence of ED in Asia, associated factors that may influence sexual attitudes and sexual behaviours, and randomized clinical trials (RCTs) of phosphodiesterase-5 (PDE-5) inhibitors to evaluate the clinical efficacy and safety of PDE-5 inhibitors in Asian men. We searched for English-language articles in MEDLINE and PubMed from January 2000 to September 2010. Our results showed that the overall reported prevalence rate of ED in Asia ranged widely, from 2% to 88%. This finding indicates that ED is a common and major health problem in this region. However, sociocultural and economic factors in Asia prevent people from seeking and obtaining appropriate medical care. We found reports on five kinds of PDE-5 inhibitors for the management of ED: sildenafil, vardenafil, tadalafil, udenafil and mirodenafil. The results of RCTs showed that these five PDE-5 inhibitors are more effective than placebo in improving erectile function in Asian men with ED and that these drugs have similar efficacy and safety profiles.
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INTRODUCTION

Erectile dysfunction (ED) has been defined as the inability to achieve or maintain an erection sufficiently rigid for achieving satisfying sexual intercourse.[1] ED is an important worldwide health issue that affects nearly half of men over the age of 40 years, and it has a significant negative impact on the quality of life and life satisfaction of the affected individual as well as his partner.[2,3] One of the most frequently cited epidemiological surveys reporting prevalence data for ED is the Massachusetts Male Aging Study.[2] The Massachusetts Male Aging Study—the first longitudinal, community-based, randomized, wide-scale epidemiological study of ED—included 1709 men between the ages of 40 and 70 years who completed a self-reported ED questionnaire. Over that age range, the probabilities of minimal, moderate and complete ED were 16.5%, 17.5% and 4.9%, respectively, at age of 40 years, and 18%, 34% and 15% at age of 70 years, showing that the prevalence of ED increases with age.

Another pivotal epidemiological study of sexual dysfunction was the Global Study of Sexual Attitudes and Behaviors (GSSAB), which included 27 500 men and women aged 40–80 years in 29 countries.[4] This study showed that physical, social/emotional and relationship factors all have a significant impact on the prevalence of ED.

The incidence of ED is higher in men with diabetes mellitus, hypertension, hypercholesterolemia, atherosclerosis or cardiovascular disease. All of these diseases and conditions are known to be associated with endothelial dysfunction.[5,6] Men who reported having at least one type of vascular disease were more likely to experience erectile difficulties.[4] In the Global Better Sex Survey, Asian men and women agreed that sex was an important part of their lives and partner relationships; however, many men may not recognize that ED is a treatable medical condition.[7]

Here we review the prevalence rate of ED in Asia, associated factors that influence sexual attitudes and sexual behaviour, help-seeking patterns, and the clinical efficacy and safety of phosphodiesterase-5 (PDE-5) inhibitors in Asian men.

PREVALENCE RATE OF ED IN ASIA

The prevalence of ED in Asian populations was recently analyzed by Cheng *et al.*[8] They performed computer-based searches through MEDLINE, PubMed, PsycINFO and other general Internet search engines for articles documenting the prevalence of ED in Asian countries between 1986 and 2006. Among the 219 relevant articles initially identified, 34 articles were retrieved, 18 of which were analyzed as general population studies. The overall reported prevalence rate of ED in Asia ranged widely, from 2% to 81.8%.[8] It was 11% in Indonesia, 19.5%–28.3% in China, 8%–50% in Hong Kong, 13%–81.1% in Japan, 22.4%–59% in Malaysia, 33%–65% in the Philippines, 2%–53% in Singapore, 18%–36.6% in South Korea, 9%–17.7% in Taiwan (China) and 29%–65% in Thailand. The prevalence of ED increased with age. The pooled random-effects age-specific prevalence rates were 15.1%, 29.6%, 40.6%, 54.3% and 70.0% for the age groups 20–29, 30–39, 40–49, 50–59 and 60–69 years, respectively. The overall, age-standardized prevalence was 36.8%. This meta-analysis showed that the prevalence rates of ED differed between countries and that there was also a wide range of overall ED prevalence

Department of Urology, Chonnam National University Medical School, Sexual Medicine Research Center, Chonnam National University, Gwangju 501-757, Korea
Correspondence: Dr K Park (uropark@gmail.com)
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in a country. The limitation of this analysis was that the tools used to evaluate ED prevalence were not the same across studies. In addition, even though the International Index of Erectile Function (IIEF) was the most frequently used assessment tool, for some of the studies a validated IIEF was not available in the local language.[8]

We searched for epidemiological studies through MEDLINE and PubMed for the period from 2001 to 2010. We reviewed 20 general population studies of ED in Asian regions (**Table 1**).[9–28] Among them, there were three important epidemiological studies of ED in Asian populations: the GSSAB subgroup study in Asian countries,[12] the Asian Men's Attitudes to Life Events and Sexuality study[11] and the Asian Survey of Aging Males.[15] The GSSAB subgroup study compared sexual behaviours, the prevalence of sexual dysfunction and help-seeking patterns in nine Asian countries. In that study, the prevalence of ED was the highest in the Philippines (33%), followed by Thailand (29%), Malaysia (28%), Korea (18%), Japan (13%), Taiwan (China) (9%), Hong Kong (China) (8%) and Singapore (2%) (**Table 1**). The Men's Attitudes to Life Events and Sexuality Phase I study consisted of 10 934 men aged 20–75 years from Mainland China, Japan, Korea, Malaysia and Taiwan (China). In that study, the self-reported prevalence of ED was the highest in Japan (14%) and the lowest in Malaysia (3%).[11] The Asian Survey of Aging Males survey was conducted in 1155 men aged 50–80 years from Hong Kong (China), Singapore, Malaysia, Philippines and Thailand. ED was reported by 63% of the participants, *via* the sexual function using Danish prostate symptom score questionnaire. The prevalence of ED was the highest in the Philippines (65%) and Thailand (65%), followed by Malaysia (59%), Singapore (53%) and Hong Kong (China) (50%). For these three studies, as shown in **Table 1**, the overall reported prevalence rates of ED in Asia ranged widely, from 2% to 88%. This high prevalence of ED indicates that ED is a common health problem in the Asian region.

Most of the other epidemiological studies in Asian regions were based on populations within a country. The majority were reported from East Asia and Southeast Asia because epidemiological data from other Asian countries are not well represented in the international database search engines. The sample sizes, age groups and assessment

Table 1 Prevalence of ED in Asian countries[9–28]

Region	*Study*	*Study size (n)*	*Age range (year)*	*Range of overall ED prevalence (%)*	*Assessment tools*
Mainland China	Bai *et al.*[9]	2226	20–86	28.4[a]	Self-report
	Lau *et al.*[10]	298	20–39	19.5	Self-report
	Tan *et al.*[11]	225	20–75	6	Self-report
	Nicolosi *et al.*[12]	250	40–80	20	Self-report
Hong Kong (China)	Wong *et al.*[13]	1566	65–92	88	IIEF
	Ng *et al.*[14]	1506	26–70	36.7	Self-report
	Li *et al.*[15]	201	50–80	50	DAN-PSS-Sex, IIEF
	Nicolosi *et al.*[12]	250	40–80	8	Self-report
Indonesia	Nicolosi *et al.*[12]	250	40–80	11	Self-report
Japan	Marumo *et al.*[16]	1517	23–79	1.0–25.9[b]	IIEF
	Sasayama *et al.*[17]	6112	30–80	32	Self-report
	Nicolosi *et al.*[18]	600	40–70	34[a]	Self-report
	Tan *et al.*[11]	228	20–75	14	Self-report
	Nicolosi *et al.*[12]	750	40–80	13	Self-report
Korea	Ahn *et al.*[19]	1570	40–79	45.8	Self-report, IIEF
	Cho *et al.*[20]	3501	>20	36.5[a]	IIEF
	Moreira *et al.*[21]	600	40–80	31.9	Self-report
	Tan *et al.*[11]	225	20–75	8	Self-report
	Nicolosi *et al.*[12]	600	40–80	18	Self-report
Malaysia	Khoo *et al.*[22]	351	>50	70.1	IIEF
	Quek *et al.*[23]	430	>20	41.6	IIEF
	Li *et al.*[15]	250	50–80	59	DAN-PSS-Sex, IIEF
	Tan *et al.*[11]	380	20–75	3	Self-report
	Nicolosi *et al.*[12]	250	40–80	28	Self-report
Philippines	Li *et al.*[15]	250	50–80	65	DAN-PSS-Sex, IIEF
	Nicolosi *et al.*[12]	250	40–80	33	Self-report
Singapore	Li *et al.*[15]	204	50–80	53	DAN-PSS-Sex, IIEF
	Tan *et al.*[24]	729	>30	51.3	IIEF
	Nicolosi *et al.*[12]	250	40–80	2	Self-report
Taiwan (China)	Hwang *et al.*[25]	1060	>30	27	IIEF, EHS, QEQ
	Wu *et al.*[26]	990	>40	26	Self-report, IIEF
	Chen *et al.*[27]	1002	>40	17.7	Self-report
	Tan *et al.*[11]	228	20–75	4	Self-report
	Nicolosi *et al.*[12]	250	40–80	9	Self-report
Thailand	Permpongkosol *et al.*[28]	2269	40–70	42.1	Self-report
	Li *et al.*[15]	250	50–80	65	DAN-PSS-Sex, IIEF
	Nicolosi *et al.*[12]	250	40–80	29	Self-report

Abbreviations: DAN-PSS-Sex, sexual function using Danish prostate symptom score; ED, erection dysfunction; EHS, erection hardness score; IIEF, International Index of Erectile Function; QEQ, quality of erection questionnaire.

[a] Age adjusted.

[b] Prevalence of ED according to age.

tools for ED were different in each study. The prevalence rate of ED varies according to the definitions and methodologies used in ED research. Therefore, future studies should be considered to collect age-specific, ED severity-specific prevalence data and to adopt an appropriate ED assessment tool with a validated cutoff value.

SEXUAL ATTITUDES AND SEXUAL BEHAVIOUR IN ASIAN MEN

The GSSAB study showed that most men and women with sexual dysfunction had not consulted a doctor about these problems.[12] This lack of communication between physician and patient is not unique to Asia; the global study showed that only 9% of men and women had been asked about their sexual health by a doctor.[29] Sexual attitudes can be influenced by cultural differences. Asian men are known to be conservative towards sex and less sexually active than Western men.[12] More specifically, the pattern of treatment-seeking behaviour differs between East and Southeast Asian regions because of cultural and religious influences. In East Asia, a Confucian cultural background predominates, whereas in Southeast Asia, people may have a Buddhist background (Thailand), a Muslim background (Malaysia and Indonesia) or a Catholic background (the Philippines). As one study reported, in Korea and other East Asian countries most patients took no action, whereas in Southeast Asia help was often sought from a partner, a family member or another source of social support[12] (**Figure 1**). Another substantial barrier to seeing a physician is the cost. Limited accessibility of medical care for financial reasons was most common in Mainland China, Indonesia and Thailand and least common in Hong Kong (China), Singapore and Japan.[12] These sociocultural and economic factors appear to prevent people from seeking and obtaining medical care. The findings imply that public awareness of ED is needed in order to encourage men to consult a physician.

MEDICAL TREATMENT OF ED IN ASIA

The first-line therapeutic option for the treatment of ED is PDE-5 inhibitors. Five types of PDE-5 inhibitors have been introduced: sildenafil, tadalafil, vardenafil, udenafil and mirodenafil. A systematic review and meta-analysis of data on oral PDE-5 inhibitors was recently reported.[30] In the 130 randomized clinical trials (RCTs) analyzed, 72 were for sildenafil, 27 were for vardenafil, 28 were for tadalafil, two were for mirodenafil and one was for udenafil. Four RCTs directly compared PDE-5 inhibitors. This study concluded that oral PDE-5 inhibitors improve erectile functioning and have similar efficacy and safety profiles.

In the current review, after a search of MEDLINE and PubMed for articles published from January 2000 to September 2010, we selected 14 Asian RCTs of PDE-5 inhibitors (**Table 2**). These included four RCTs of sildenafil,[31–34] two RCTs of vardenafil,[35,36] four RCTs of tadalafil,[37–40] two RCTs of udenafil[41,42] and two RCTs of mirodenafil.[43,44] The efficacy and safety of two novel PDE-5 inhibitors, mirodenafil and udenafil, were evaluated only in Korean men. In this review, we did not include clinical trials of PDE-5 inhibitors in men with specific comorbid diseases, such as diabetes, hypertension and other neurovascular diseases.

Efficacy and safety of sildenafil

Of the five PDE-5 inhibitors, sildenafil was the first to be launched in Asia. Three multinational or multi-institutional studies, collectively called the Asian Sildenafil Efficacy and Safety Study (ASSESS), have evaluated the efficacy, safety and tolerability of oral sildenafil in Asian men with ED with broad-spectrum aetiology.[31–33] The ASSESS-1 trial was carried out at eight centres in Malaysia, the Philippines and Singapore.[31] ASSESS-2 was performed in four centres in Thailand[32] and ASSESS-3 was conducted in Taiwan (China).[33] In these three studies, a total of 616 Asian men were randomly assigned to 12 weeks of sildenafil or placebo taken as needed 1 h before anticipated sexual activity. Initially, the sildenafil or matching placebo dose was 50 mg but could be increased to 100 mg or decreased to 25 mg depending on efficacy or intolerance, respectively. The primary efficacy variables related to achievement and maintenance of erections sufficient

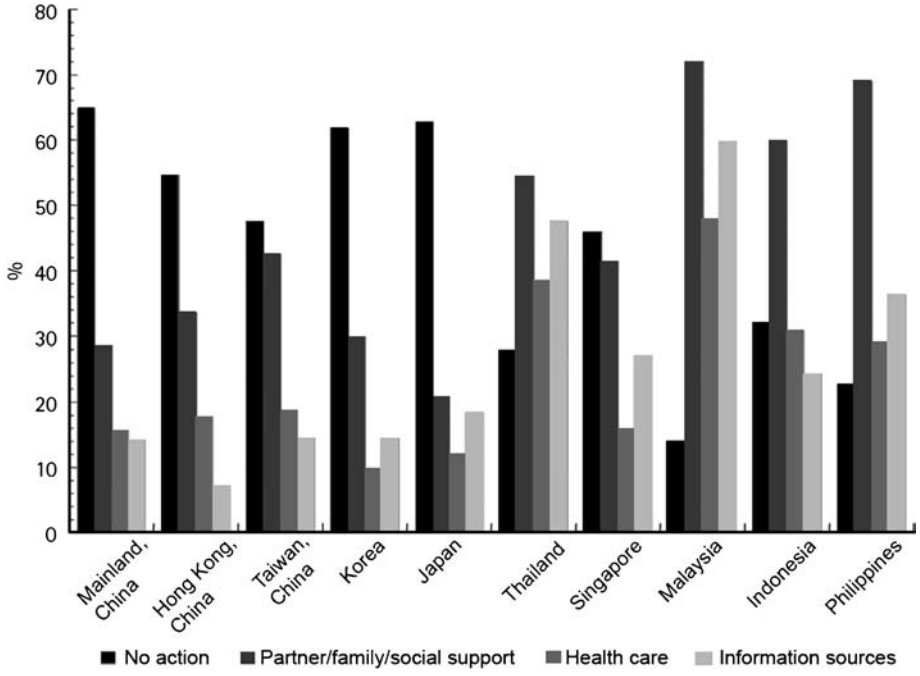

Figure 1 Help-seeking behaviour of men and women with sexual dysfunction in Asia as determined by the GSSAB, 2001–2002.[12] Adapted with permission. GSSAB, Global Study of Sexual Attitudes and Behaviors.

Table 2 Studies evaluating PDE-5-I administration for ED in Asian men[31–44]

Study	*Drug*	*Study design*	*Patients*	*Outcome measures*	*Efficacy*	*Adverse event*
Tan *et al.*[31]	Sildenafil versus placebo (50 mg increased to 100 mg or decreased to 25 mg) for 12 weeks	Multinational, multi-institutional randomized controlled trial	254 men; aged 26–78 years; ED duration >6 months	IIEF, patients' event logs of sexual activity, and a global efficacy question	Higher EF with sildenafil than with placebo, IIEF Q3 (4.22 versus 2.59) and Q4 (4.15 versus 2.41) ($P<0.0001$), significantly improved IIEF-EF and GEAQ in sildenafil group ($P<0.0001$)	22.8% of sildenafil versus 10.2% of placebo; flushing, dizziness and headache
Kongkanand *et al.*[32]	Sildenafil versus placebo (50 mg increased to 100 mg or decreased to 25 mg) for 12 weeks	Multi-institutional randomized controlled trial in Thailand	125 men; aged 26–77 years; ED duration >6 months	IIEF, patients' event logs of sexual activity, and a global efficacy question	Higher EF with sildenafil than with placebo, successful attempts at sexual intercourse (66.16% versus 33.05%)	30.2% of sildenafil versus 11.3% of placebo; flushing, dizziness and headache
Chen *et al.*[33]	Sildenafil versus placebo (50 mg increased to 100 mg or decreased to 25 mg) for 12 weeks	Multi-institutional randomized controlled trial in Taiwan	236 men; aged 26–80 years; ED duration >6 months	IIEF, patients' event logs of sexual activity, and a global efficacy question	Higher EF with sildenafil than with placebo, IIEF Q3 (4.17 versus 2.98) and Q4 (4.14 versus 2.88) ($P<0.0001$), significantly improved IIEF-EF and GEAQ in sildenafil group ($P<0.0001$)	43.7% of sildenafil versus 18.8% of placebo; flushing, dizziness and headache
Choi *et al.*[34]	Sildenafil versus placebo (50 mg increased to 100 mg or decreased to 25 mg) for 8 weeks	Multi-institutional randomized controlled trial in Korea	133 men; aged 28–78 years; ED duration >6 months	IIEF, patients' event logs of sexual activity, and a global efficacy question	Higher EF with sildenafil than with placebo, IIEF Q3 (4.19 versus 2.67) and Q4 (3.74 versus 2.07) ($P<0.0001$), significantly improved IIEF-EF and GEAQ in sildenafil group ($P<0.0001$)	56.1% of sildenafil versus 20.9% of placebo; flushing, headache and abnormalities in colour vision
Tan *et al.*[35]	Vardenafil (10 mg) versus placebo for 12 weeks	Multinational, multi-institutional randomized controlled trial	358 men; aged ⩾20 years; ED duration >6 months	IIEF-EF domain score, success rate of vaginal penetration (SEP2), penile rigidity (SEP3), GAQ	Increased IIEF-EF scores in vardenafil compared with placebo (22.4 versus 14.3, $P<0.001$), improved SEP2 (82.2 versus 43.6, $P<0.001$), SEP3 (66.1 versus 24.0, $P<0.001$), positive GAQ responses (81.8% versus 24.3%)	25.4% of the vardenafil group, the majority mild and transient headache, flushing, nasal congestion and dizziness
Chen *et al.*[36]	Vardenafil (10 mg) versus placebo for 12 weeks	Multinational, multi-institutional randomized controlled trial	306 men; aged ⩾20 years; ED duration >6 months	IIEF-EF domain score, success rate of vaginal penetration (SEP2), penile rigidity (SEP3), GAQ	Greater increase in IIEF-EF score in vardenafil group compared with placebo (24.2 versus 15.9), higher SEP2 (88% versus 58%), higher SEP3 (69% versus 23%), higher positive GAQ responses (85% versus 33%)	54.2% of vardenafil versus 43.0% of placebo; mild intensity flushing, rhinitis and headache
Yip *et al.*[37]	Tadalafil (20 mg) versus placebo for 12 weeks	Multinational, multi-institutional randomized controlled trial	242 men; aged >18 years; ED duration >3 months	IIEF, SEP diary, GAQ	Significantly improved EF in tadalafil compared with placebo ($P<0.001$), greater SEP3 (70.9% versus 33.5%), greater GAQ (86.2% versus 30.1%)	Headache (11.3%), back pain (7.5%), dizziness (3.8%) and dyspepsia (3.1%)
Guo *et al.*[38]	Tadalafil (10 or 20 mg) versus placebo for 12 weeks	Multinational, multi-institutional randomized controlled trial	367 men; aged >18 years; (>21 in Singapore) ED duration >3 month	IIEF, SEP diary, GAQ	Tadalafil 10 and 20 mg improve IIEF (8.1 and 8.7, versus placebo 2.4, $P<0.001$), SEP3 (62% and 70%, placebo 32%, $P<0.001$), GAQ (81% and 86% versus 44%, $P<0.001$)	Headache, back pain, dyspepsia and dizziness

To be continued

Table 2 (Continued) Studies evaluating PDE-5-I administration for ED in Asian men[31–44]

Study	*Drug*	*Study design*	*Patients*	*Outcome measures*	*Efficacy*	*Adverse event*
Chen *et al.*[39]	Tadalafil (10 or 20 mg) versus placebo for 12 weeks	Multi-institutional randomized controlled trial in Taiwan	196 men; aged >21 years; ED duration >3 months	IIEF, SEP diary, GAQ	Tadalafil improved EF compared with placebo ($P<0.005$), SEP Q3: 70.0%, 10 mg; 78.0%, 20 mg versus 42.8% placebo, GAQ: 92.3% and 84.6% versus 54.5% placebo	Back pain, dyspepsia and myalgia
Guo *et al.*[40]	Tadalafil (10 or 20 mg) versus placebo for 12 weeks	Integrated analysis of five double-blind, placebo-controlled trials	1046 men; aged >18 years; ED duration >3 months	IIEF, SEP diary, GAQ	Tadalafil 10 or 20 mg improved IIEF-EF ($P<0.001$), better SEP Q3 (64.1%, 70.5% versus placebo 33.4%, $P<0.001$), improved GAQ (85.5%, 85.4% versus placebo 43.5%, $P<0.001$)	1.3% of tadalafil versus 1.1% of placebo; headache and back pain
Paick *et al.*[41]	Udenafil (100 or 200 mg) versus placebo for 12 weeks	Multi-institutional randomized controlled trial in Korea	167 men; aged 19–70 years; ED duration >6 months	IIEF, SEP diary, GAQ	Significantly improved IIEF-EF, SEP Q2 and SEP Q3 ($P<0.0001$), GAQ (placebo, 25.9%; udenafil 100 mg, 81.5%; udenafil 200 mg, 88.5%, $P<0.0001$)	Flushing, headache and nasal congestion
Park *et al.*[42]	Udenafil (100 mg) versus placebo for 4 weeks	Multi-institutional randomized controlled trial in Korea	103 men; aged 19–70 years; ED duration >6 months	IIEF-EF domain score, SEP2, SEP3	Enhanced SEP Q3 (placebo, 28.3% versus udenafil, 54.7%; $P<0.0001$), significant change from base line in IIEF-EF (placebo, 0.58; udenafil, 4.40; $P<0.0001$)	4% of placebo, 11.3% of udenafil; flushing, headache and toothache
Paick *et al.*[43]	Mirodenafil (SK3530; 50, 100 or 150 mg) versus placebo for 8 weeks	Multi-institutional randomized controlled trial in Korea	119 men; aged 19–70 years; ED duration >6 months	IIEF, SEP diary, GAQ	All primary and secondary efficacy end points significantly improved ($P<0.05$) 42.3% achieved normal erectile function after treatment	Flushing, headache, dizziness and eye redness (10.9%, 7.6%, 2.5% and 2.5%, respectively)
Paick *et al.*[44]	Mirodenafil (50 or 100 mg) versus placebo for 12 weeks	Multi-institutional randomized controlled trial in Korea	223 men; aged 19–70 years; ED duration >6 months	IIEF, SEP diary, GAQ, LSC	Mirodenafil 50 and 100 mg, greater increase in IIEF Q3, Q4 ($P<0.0001$), improved IIEF-EF, SEP2, SEP3, GAQ and LSC	Mild intensity flushing, headache, nausea and eye redness

Abbreviations: ED, erectile dysfunction; EF, erectile function; IIEF, International Index of Erectile Function; GAQ, global assessment question; GEAP, global efficacy assessment question; LSC, life satisfaction checklist; PDE-5, phosphodiesterase-5; SEP, sexual encounter profile.

for sexual intercourse and the secondary efficacy variables, such as IIEF-EF domains, the percentage of successful intercourse attempts and the global assessment of erections, were all statistically significantly improved by sildenafil as compared with placebo. In one trial, only the sexual-desire domain showed no significant difference.[32] These results demonstrate that sildenafil is effective in restoring sexual function in Asian men with ED of various aetiologies. The other RCT of sildenafil, the ASSESS-K study, was a flexible-dose escalation study performed at six centres in Korea.[34] ASSESS-K was similar to the other ASSESS studies except for a shorter trial period (8 weeks). In all four studies, common adverse events with sildenafil were flushing, dizziness and headache, most of which were mild.

Efficacy and safety of vardenafil

Two prospective, randomized, double-blind, placebo-controlled, fixed-dose, parallel-group studies have been conducted to assess the safety and efficacy of vardenafil 10 mg for the treatment of ED in Asian regions.[35,36] The first such study was performed in six countries or regions: Malaysia, Singapore, Thailand, the Philippines, Hong Kong (China) and Indonesia.[35] In this study, 358 men with ED were randomly assigned to receive vardenafil 10 mg or placebo for 12 weeks. The primary efficacy variables were the IIEF-EF and the sexual encounter profile (SEP) questions related to penetration (SEP2) and intercourse completion (SEP3). Secondary efficacy variables were the global assessment question (GAQ) regarding erection improvement.

Treatment with vardenafil significantly improved the IIEF-EF domain scores as compared with placebo (22.4 versus 14.3; $P<0.001$) and also improved SEP2 (vardenafil 82.2 versus placebo 43.6; $P<0.001$) and SEP3 (vardenafil 66.1 versus placebo 24.0; $P<0.001$). Positive GAQ responses were reported by 81.8% of the participants in the vardenafil group and 24.3% of those in the placebo group. The most frequent adverse events were headache, flushing, nasal congestion and dizziness.

The other vardenafil study was conducted in 306 men with ED in Taiwan, South Korea and Japan.[36] Treatment with vardenafil produced significant improvement in the main efficacy measures of IIEF-EF score and SEP2 and SEP3 as well as the GAQ. The efficacy

and safety of vardenafil in East Asian men were similar to those reported in previous studies of Western populations.[45,46]

Efficacy and safety of tadalafil

Tadalafil is considered an effective, well-tolerated therapy for Asian men with ED of broad-spectrum severity and aetiology.[37–40,47] Yip *et al.*[37] assessed the efficacy and safety of tadalafil as compared with a placebo in a multicentre, randomized, double-blind, parallel-group, placebo-controlled study conducted at 17 centres across East and Southeast Asia: Hong Kong (China) (one site, 38 patients), Indonesia (two sites, 21 patients), Malaysia (three sites, 32 patients), the Philippines (four sites, 40 patients), Singapore (three sites, 30 patients) and Taiwan (China) (four sites, 81 patients). In this study, men older than 18 years with mild to severe ED of various aetiologies were randomly assigned to receive a placebo or 20 mg tadalafil taken as needed. Tadalafil significantly improved erectile function as compared with placebo ($P<0.001$). At the end point, the tadalafil group reported successful intercourse attempts (SEP3: 70.9% compared with 33.5% in the placebo) and improved erections (GAQ: 86.2% compared with 30.1%). The most common treatment-emergent adverse events were headache, back pain, dizziness and dyspepsia.

Tadalafil was also shown to be an effective and well-tolerated treatment for Southeast Asian men with ED.[38,39] In these studies, the study design was a randomized, double-blind, placebo-controlled study of men with mild to severe ED of various aetiologies who were randomly assigned to receive placebo, tadalafil 10 mg or tadalafil 20 mg taken as needed without restrictions on food intake and timing of sexual activity for 12 weeks. Tadalafil RCTs were conducted in 10 centres across Mainland China, Singapore and the Philippines[38] ($n=367$) and eight centres in Taiwan (China)[39] ($n=196$). Compared with placebo, tadalafil significantly improved erectile dysfunction on all efficacy outcomes ($P<0.001$). The most common adverse events reported by patients were headache, back pain, dyspepsia and dizziness.

Guo *et al.*[40] conducted an integrated analysis of five Asian tadalafil clinical trials involving 1046 patients and determined the efficacy and safety of tadalafil in diverse clinical populations with comorbid medical conditions. In this study, patients receiving 10 mg or 20 mg tadalafil, as compared with patients receiving placebo, showed significant improvement from baseline to the end point in the IIEF-EF domain score in all clinical subpopulations ($P<0.001$). The 10 mg and 20 mg tadalafil groups showed mean success rates of 64.1% and 70.5%, respectively, for SEP3, as compared with 33.4% in the placebo group ($P<0.001$). Also, 85.5% and 85.4%, respectively, reported improved erections on the end point GAQ versus 43.5% in the placebo group ($P<0.001$). Tadalafil was well tolerated across all groups, and the most frequently reported adverse events were headache and back pain.

Efficacy and safety of udenafil

Udenafil (Zydena®, Dong-A Phamaceutical, Seoul, Korea) is a newly developed, potent, selective PDE-5 inhibitor that can also inhibit cyclic guanosine monophosphate hydrolysis.[48] Its pharmacokinetic profile includes unique clinical properties of both a relatively rapid onset and a long duration of action.[49] In addition, the isoenzyme selectivity profile of udenafil is similar to that of sildenafil. On the other hand, unlike tadalafil, it does not inhibit PDE-11. In a multicentre, double-blind, placebo-controlled, fixed-dose, parallel-group phase III trial, 167 Korean patients with ED of diverse origin and severity were randomly assigned to take placebo or udenafil at fixed doses of 100 mg or 200 mg as needed for 12 weeks.[41] The efficacy of udenafil was assessed by IIEF-EF domain scores, SEP2, SEP3 and GAQ. The patients treated with udenafil showed a significantly greater change from baseline in the IIEF-EF domain score as compared with those given placebo (placebo, 0.20; 100 mg udenafil, 7.52; and 200 mg udenafil, 9.93) ($P<0.0001$). Udenafil significantly enhanced SEP2 and SEP3 as compared with placebo ($P<0.0001$). The GAQ also increased significantly in the udenafil group as compared with the placebo group (GAQ: 100 mg udenafil, 81.5%; 200 mg udenafil, 88.5%; and placebo, 25.9%) ($P<0.0001$). These results indicate that udenafil is an effective and well-tolerated therapy for ED of broad-spectrum aetiology and severity. The most common treatment-related adverse events were facial flushing and headache.

Another RCT evaluated the efficacy of udenafil in treating ED for up to 12 h after dosing.[42] This study was performed to evaluate the duration of udenafil efficacy for sexual intercourse. Udenafil significantly enhanced the SEP3 (placebo 28.3% versus udenafil 54.7%; $P<0.0001$) and IIEF-EF domain from baseline, whereas there was no significant difference in the SEP2 between the two groups. These data suggest that udenafil may be a reliable treatment option in patients who have relatively spontaneous and unscheduled sexual intercourse.

Efficacy and safety of mirodenafil

Mirodenafil (SK3530) is a newly developed oral PDE-5 inhibitor for the treatment of ED.[43] Preclinical studies revealed that SK3530 has selectivity comparable with that of conventional PDE-5 inhibitors.[43,50] Paick *et al.*[43] evaluated the efficacy and safety of mirodenafil in a total of 119 patients randomized at 10 centres in Korea. The patients received either mirodenafil (50, 100 or 150 mg) or placebo for an 8-week period. The efficacy of mirodenafil was assessed using the IIEF, SEP and GAQ. At the end of the study, all primary and secondary efficacy end points were statistically significantly improved by mirodenafil as compared with placebo ($P<0.05$). The most common adverse events were flushing, headache, dizziness and redness of the eyes (10.9%, 7.6%, 2.5% and 2.5%, respectively), and most were mild.

A consecutive clinical study of mirodenafil was conducted with 223 subjects who were randomly assigned to placebo or mirodenafil at fixed doses of 50 or 100 mg for 12 weeks.[44] The mirodenafil 50 and 100 mg groups showed a significantly greater increase in the scores for IIEF question 3 regarding the availability of penile penetration to partner ($P=0.0001$ and $P<0.0001$, respectively) and question 4 (both $P<0.0001$) at the end point as compared with the placebo group. Mirodenafil in both doses significantly improved the IIEF, SEP2 and SEP3 scores and the GAQ as compared with placebo. The most frequent adverse events were facial flushing, headache, nausea and redness of the eyes.

CONCLUSION

The prevalence rate of ED in Asia ranged widely, from 2% to 88%. This finding indicates that ED is a common and major health problem in this region. However, sociocultural and economic factors in Asia prevent people from seeking and obtaining appropriate medical care. Five kinds of PDE-5 inhibitors for the treatment of ED have been studied in Asian countries: sildenafil, vardenafil, tadalafil, udenafil and mirodenafil. The results of RCTs have shown that these five PDE-5 inhibitors are more effective than placebo in improving erectile function in Asian men with ED. The adverse events reported by patients tended to be mild or moderate in severity, and the rate of discontinuation caused by

adverse events was similar to those observed in Western countries. Further well-designed, long-term PDE-5 inhibitor trials are needed to evaluate their efficacy and safety in the presence of comorbid conditions or specific causes of ED.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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