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Phosphodiesterase type 5 inhibitors: Irrational use in Saudi Arabia

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Abstract *Objective:* To identify the criteria of phosphodiesterase type 5 inhibitor (PDE5i) users and to analyse the knowledge, attitude, and practices of PDE5i use amongst Saudi men.

Subjects and methods: A web-based, cross-sectional survey was conducted in Saudi Arabia between January and April 2015. Sexually active adult men were inter-viewed using a website questionnaire designed by the authors. Descriptive statistics were used to analyse the data.

Results: In all, 1008 men participated in the survey with 378 (37.5%) reporting use of PDE5i. Of those using PDE5i, 144 (38.1%) reported erectile dysfunction and 234 (61.9%) reported normal erection (recreational users). We found several demographic features, including high education level, health field occupation, high income, smoking, and increased frequency of sexual intercourse amongst the PDE5i users. Most of the PDE5i users (92.3%) had knowledge about PDE5i and 84.1% of them bought it without medical prescription. The most commonly used PDE5i was tadalafil (46.1%) and most of the users (79.9%) reported improvement in their sex-ual activity after PDE5i usage. Amongst the recreational users, the main reasons for

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PDE5i usage were curiosity (38.5%) and improving self-confidence (25.6%). Of them, 69.2% reported benefits from PDE5i usage, mainly in the form of enhancement of erection (36.7%) and increasing erection duration (31.2%).

Conclusion: PDE5i use appears to be frequent in Saudi Arabia. Most of the users had knowledge about PDE5i and claimed to get benefits from it, even if used as a recreational drug.

Introduction

Erectile dysfunction (ED) is a common health problem affecting men worldwide. It is defined as repeated inability to get or maintain an erection sufficient for intercourse. Whilst ED is not a life-threatening problem, its effect on quality-of-life issues is significant [1]. There are various treatment options available for ED. Amongst these options is phosphodiesterase type 5 inhibitor (PDE5i) oral therapy (namely: sildenafil, tadalafil, and vardenafil) [2], which act by inhibiting the PDE5 enzymes and thereby facilitate erection [3,4].

Currently, PDE5i is the most well tolerated and effective class of medications for treatment of ED. However, their misuse by men without ED is considered a public health concern. Undoubtedly, they have become some of the most abused pharmaceuticals and their recreational use has greatly exceeded their medical use [5–8]. Previous studies have shown that the use of PDE5i is associated with the use of other illegal or illicit drugs, alcohol abuse, and risky sexual behaviours with a higher rate of recent sex partners and sexually transmitted disease [7,8]. However, there is a possible difference in cultural beliefs and sexual behaviours in different countries, so we cannot extrapolate these findings to the local community.

Due to the fact that there are scanty local data on the use of PDE5i and reticence in discussing sexual practice in our environment, we conducted this research through a website survey. The aim was to investigate the use of PDE5i in the Saudi population, and to identify the criteria of the users, either for those intended to treat ED or recreational users. Additionally, the knowledge, attitude, and practices of PDE5i use were analysed.

Subjects and methods

A cross-sectional, descriptive study was carried out in Saudi Arabia via a web-based survey between 1 January and 1 April 2015. The participants were recruited by an invitation distributed through direct e-mail and social media. The targeted population was non-specific and included all sexually active Saudi men aged ⩾18 years. Because the data were to be based on an observational web-based survey, we did not set strict exclusion criteria, except for age and sexual activity. All participants provided informed consent and voluntarily reported their private information.

The survey gathered 36 open and closed questions designed to measure the following domains: demographics, lifestyle, health problems, sexual behaviours, erectile function, ejaculation, sexual satisfaction, sexual dysfunction treatment, and use of PDE5i. For the purpose of this study, participants with a history of PDE5i usage were subjected to additional questions to collect data about: type of PDE5i used, acquisition method, reasons for its use, and its effect. Also the knowledge and perception of the participants towards PDE5i were assessed by separate questions. Erectile function was assessed using a validated Arabic version of the five-item version of the International Index of Erectile Function (IIEF-5) questionnaire and a score of ⩽21 was used to define ED [9]. The International Society for Sexual Medicine (ISSM) definition of premature ejaculation 'ejaculation which always or nearly always occurs prior to or within about one minute from the beginning of sexual intercourse' was used to define premature ejaculation [10].

A preliminary pilot study was conducted with 30 sexually active men to determine the validity of the questions. The opinion of the researchers was sought and adjustment was made before induction of the survey. The local Institutional Review Board Committee of our institute approved the study project and all collected data were anonymous and confidential, and used for research purposes only.

Based on the response to the IIEF-5 questionnaire, PDE5i users were divided into two groups: ED group and recreational users group (normal erection group). The following variables were evaluated and compared between both groups: age, education level, occupation sectors, household income, smoking, chronic medical diseases, use of regular medications, number of sex partners, duration of sexual activity, frequency of sexual intercourse, erection level (graded from 1 to 5, as assessed by the IIEF-5 questionnaire), ejaculation problems, overall sexual satisfaction level (graded from 1 'unsatisfied' to 5 'fully satisfied' as self-reported by the participants), previous medical consultation for sexual problems, main sources of knowledge about PDE5i and reasons for its use, type of PDE5i used and reported

effect, and adverse events (AEs). Additionally, the PDE5i recreational users were subjected to sub-analysis to evaluate their attitude and perception of the medications.

Sample size calculation and statistical analysis

The sample size was calculated using the formula: sample size = $Z_{1-\alpha/2}2p(1-p)/d^2$ (where $Z_{1-\alpha/2}$ is the value of normal deviation at the considered level of confidence, p is the expected prevalence in the study group, and d is the expected absolute allowable error in the estimate). According to previous published studies [11,12], we assumed 22% prevalence of recreational use of PDE5i. After addition of a 6% expected allowable error, a minimum of 350 samples were required to provide a power of 0.90 and a two-sided I error of 0.05. All statistical analyses were carried out using SPSS software (SPSS Inc., Chicago, IL, USA). The continuous data are presented as the median and range, and categorical data as the number and percentage. The Mann–Whitney U-test was used to compare continuous data and chi-squared or Fisher's exact test was used to compare categorical data. The relationship between age and frequency of sexual intercourse was measured using the Spearman's rank correlation coefficient.

Results

In all, 1008 sexually active men with a legitimate sex partner completed the survey. Of those, 402 (39.9%) reported the usage of sex-enhancing medications in the form of herbal or PDE5i during their lifetime. Excluding the participants taking herbal medications, the reported frequency of PDE5i usage was 37.5% (378/1008). From the PDE5i users, 144 (38.1%) had ED and 234 (61.9%) had normal erections (recreational users).

The median (range) age of the entire PDE5i users was 39 (18–73) years and most of them (71.4%) were aged > 35 years. Various features that might affect PDE5i habituation and/or erectile function were present: high school education level (71.4%), health field occupation (23.8%), high household income (58.7%), smoking (44.4%), history of comorbidities (34.9%), and use of regular medications (34.1%). Comparing PDE5i recreational users with those with ED, they had higher school

Table 1 Demographic and clinical characteristics of PDE5i users.

Variable	Total	ED group	Recreational group	P
Number of men	378	144	234	
Age, years				0.387
Median (range)	39 (18–73)	40 (18–73)	39 (26–57)	
Age groups, n (%)				
18–25	18 (4.8)	18 (12.5)	0	
26–30	30 (7.9)	24 (16.7)	30 (12.8)	
31–35	60 (15.9)	0	36 (15.4)	
36–40	102 (27.0)	36 (25.0)	66 (28.2)	
41–45	36 (9.5)	18 (12.5)	18 (7.7)	
>45	132 (34.9)	48 (33.3)	84 (35.9)	
School education level, n (%)				
Low	12 (25.4)	6 (4.2)	6 (2.6)	0.575
Middle	96 (3.2)	54 (37.5)	42 (17.9)	<0.001
High	270 (71.4)	84 (58.3)	186 (79.5)	<0.001
Household income, n (%)				
Low	12 (3.2)	12 (8.3)	0	<0.001
Middle	144 (38.1)	66 (45.8)	78 (33.3)	0.020
High	222 (58.7)	66 (45.8)	156 (66.7)	<0.001
Smoking, n (%)	168 (44.4)	60 (41.7)	108 (46.2)	0.394
Co-morbidities, n (%)				
Hyperlipidaemia	42 (11.1)	18 (12.5)	24 (2.6)	0.613
Diabetes mellitus	30 (7.9)	24 (16.7)	6 (10.3)	<0.001
Cardiovascular disease	6 (1.6)	6 (4.2)	0	0.003
Others	19 (5.0)	11 (7.6)	8 (3.4)	0.114
>1 health problem	35 (9.3)	25 (17.4)	10 (4.3)	<0.001
Medications affecting potency, n (%)				
Anti-hyperlipidaemics	40 (10.6)	18 (12.5)	22 (9.4)	0.436
Anti-diabetics	30 (7.9)	24 (16.7)	6 (2.6)	<0.001
Antacids	8 (2.1)	5 (3.5)	3 (1.3)	0.269
Anti-hypertensives	6 (1.6)	6 (4.2)	0	0.003
Others	11 (2.9)	6 (4.2)	5 (2.1)	0.409
Multiple medications	35 (9.3)	25 (17.4)	10 (4.3)	<0.001

education level (79.5% vs 58.3%) and household income (66.7% vs 45.8%) with lower rates of multiple comorbidities (4.3% vs 17.4%), diabetes mellitus (10.3% vs 16.7%) and cardiovascular disease (0.0% vs 4.2%). The demographic and clinical characteristics of the entire cohort of PDE5i users, ED and recreational users' subgroups are summarised in Table 1.

Amongst the 378 PDE5i users, 92.1% had constant sexual activity with one sex partner and more than half of them (56.1%) had had a regular sexual relationship for >10 years. Overall, 77.8% of the PDE5i users had no history of medical consultation for any sexual problems and most of them (87.6%) were not fully satisfied by their sexual activity. The PDE5i recreational users had lower rates of ejaculation problems and higher sexual satisfaction levels than those using PDE5i due to ED (30.8% vs 50.0% and 17.9% vs 4.2%, respectively; Table 2).

Fig. 1A and B shows the frequency of sexual intercourse amongst the PDE5i users. Most of the PDE5i users (77.8%) had an intercourse frequency >2/week. There was a significant negative relationship between frequency of sexual intercourse and age (r −0.166; $P = 0.001$). This overall significant negative relationship was seen in the PDE5i recreational users (r −0.234; $P < 0.001$) and not in those with ED (r −0.042; $P = 0.617$). However, when the study populations were stratified by age categories, this significant negative relationship was seen in each respective age category, overall and in both groups.

The PDE5i that the participants reported using were tadalafil (46.1%), sildenafil (20.6%), vardenafil (3.2%), and more than one type (30.2%); most of the

participants using more than one type of PDE5i were recreational users (84/114, 73.7%).

Most of the users (84.1%) purchased the PDE5i from drug stores without medical prescription. In all, 92.3% of PDE5i users were aware of the nature of the drug used, and the main sources of knowledge were: (a) friends and community, 49.2%; (b) media, 34.9%; (c) books and magazines, 12.7%; and (d) websites, 3.2%. At least one of the drug side-effects was reported by 31.7% of the PDE5i users and most of them (79.9%) reported improvement of sexual activity.

PDE5i recreational users sub-analysis

Amongst the recreational users, the main reasons of drug usage were: (a) curiosity, 38.5%; (b) enhancing self-confidence, 25.6%; (c) increasing erection duration, 10.3%; and (d) improving ejaculation problems, 5.1%. All the recreational users bought the PDE5i, mainly from drug stores (73.9%), without a medical prescription. PDE5i acquisition difficulties were reported by 25.6% of recreational users and the main causes were shyness (60%), fear of drug side-effects (26.7%), pharmaceutical refusal (8.3%), and cost (5.0%). Out of 234 men, 162 (69.2%) reported improvement of sexual function, mainly in the form of enhancement of erection (36.7%) and increasing erection duration (31.2%). No major drug-related AEs were reported. With respect to recommendation, only 23.1% of recreational users were given advice about PDE5i usage without medical indications. Other acquisition proprieties and the reported benefits and AEs of PDE5i recreational users are summarised in Table 3.

Table 2 Sexual characteristics of PDE5i users. Data are presented as n (%).

Variables, n (%)	Total ($n = 378$)	ED group ($n = 144$)	Recreational group ($n = 234$)	P
Number of sex partners				
1	348 (92.1)	132 (91.7)	216 (92.3)	0.823
⩾2	30 (7.9)	12 (8.3)	18 (7.7)	
Duration of sexual activity				0.302
1 year	24 (6.3)	12 (8.3)	12 (5.1)	
1–5 years	68 (18.0)	30 (20.8)	38 (16.2)	
5–10 years	74 (19.6)	24 (16.7)	50 (21.4)	
>10 years	212 (56.1)	78 (54.2)	134 (57.3)	
Ejaculation problem				
Premature ejaculation	108 (28.6)	60 (41.7)	48 (20.5)	<0.001
Delayed ejaculation	36 (9.5)	12 (8.3)	24 (10.3)	0.661
Previous medical consultation for sexual problem				0.308
No	294 (77.8)	108 (75.0)	186 (79.5)	
Yes	84 (22.2)	36 (25.0)	48 (20.5)	
Sexual satisfaction level				<0.001
1 (unsatisfied)	18 (4.8)	12 (8.3)	6 (2.6)	
2	36 (9.5)	30 (20.8)	6 (2.6)	
3	168 (44.4)	78 (54.2)	90 (38.5)	
4	108 (28.6)	18 (12.5)	90 (38.5)	
5 (satisfied)	48 (12.7)	6 (4.2)	42 (17.9)	

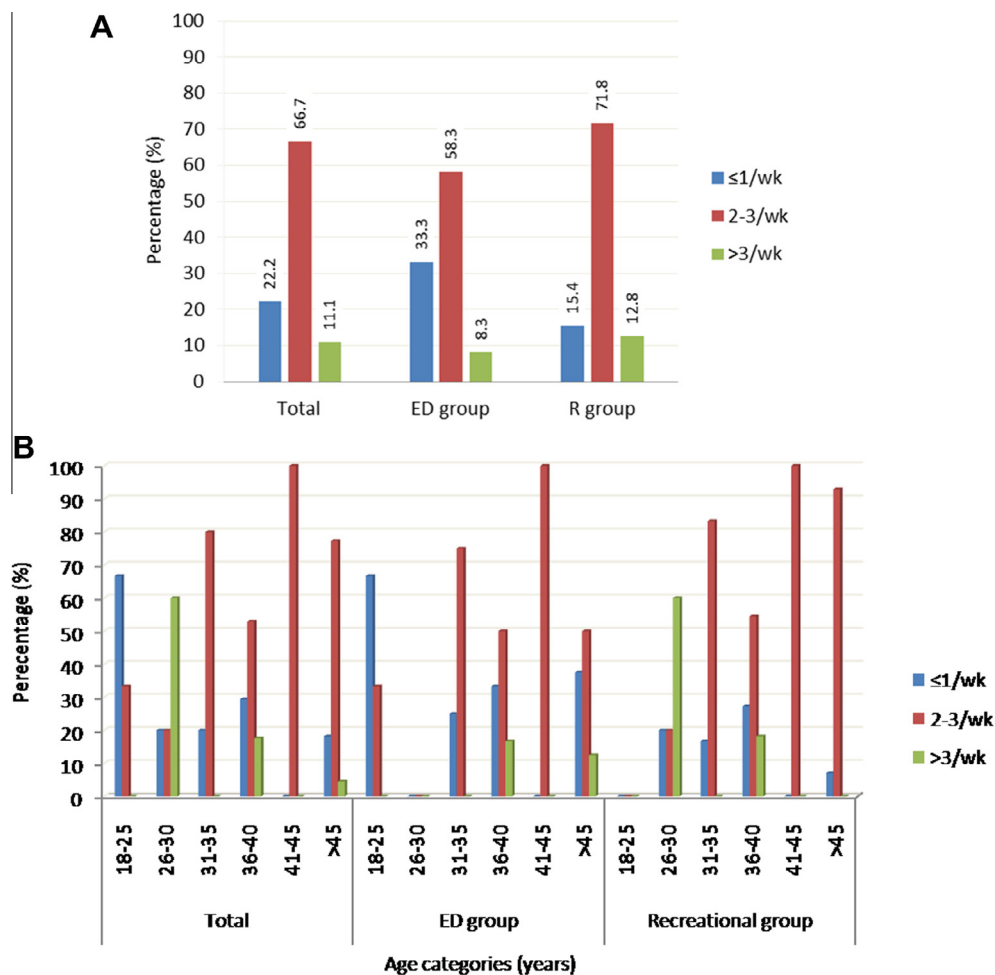**Figure 1**   (A) The frequency (≤1/week vs 2–3/week vs >3/week) of sexual intercourse amongst PDE5i users. R group, recreational-user group. (B) The frequency (≤1/week vs 2–3/week vs >3/week) of sexual intercourse amongst PDE5i users stratified by age group.

Discussion

Shortly after sildenafil was launched in 1998, authors started to report its recreational use [7]. For the last decade, an increasing number of young men without a definite diagnosis of ED are taking PDE5i, aiming to increase their sexual performance. Several studies [8,11–13] reported the use of the PDE5i by young healthy men (mostly college students) without any medical indication. One of the problems of buying PDE5i without prescription is lacking knowledge about contraindications and existing co-morbidities. The present study investigated the criteria of PDE5i users in a Saudi population, whether their usage was intended to treat ED or was on a recreational basis.

Amongst the 1008 sexually active men who participated in the present survey, 37.5% reported PDE5i usage and there were more recreational users than those who used PDE5i because of their ED (61.9% vs 38.1%). Also, most of the PDE5i users consumed the drug without medical control. This is consistent with other studies that showed that most of their respondents got their ED

medications from a non-healthcare provider source [14–16]. In their study of 4428 male twins and their siblings, Santtila et al. [16] attributed this to the young age of their participants who had a mean age of <30 years. This is different from our present study participants who had a median (range) age of 39 (18–73) years and most of them (71.4%) were aged > 35 years.

In their study of 60 healthy patients aged 20–40 years, Mondaini et al. [17] stated that sildenafil does not improve erection in healthy individuals. That is different from what was reported by 69.2% of the recreational users in our present study, in that PDE5i improved sexual performance manifested by enhancement of erection or increasing erection duration. This difference may be attributable to our larger sample of participants, in addition to the expected role of psychological factors affecting the final judgment reported by the study participants. However, as it is well known that PDE5i has potential immediate deleterious effects and due to lack of studies on their long-term effects, we cannot recommend its recreational use without medical control.

Table 3 PDE5i acquisition properties and the reported benefits and AEs amongst 234 recreational users.

Variable	N (%)
Source	
Drug stores	173 (73.9)
Friends	46 (19.7)
Drug representatives	15 (6.4)
Form	
Tablet/capsule	150 (64.1)
Full package	84 (35.9)
Frequency	
Weekly	6 (2.6)
Monthly	24 (10.3)
Irregular	204 (87.2)
Impression of the cost	
Reasonable	84 (35.9)
Cheap	6 (2.6)
Expensive	144 (61.5)
Benefits	
None	72 (20.5)
Enhancement of penile rigidity	86 (36.7)
Increasing erection duration	73 (31.2)
Self confidence	51 (21.8)
Sense of warmth	42 (17.9)
Increasing sexual desire	25 (10.7)
AEs	
None	180 (76.9)
Nasal congestion	25 (10.7)
Flushing	16 (6.8)
Headache	13 (5.6)
Palpitation	10 (4.3)
Back pain	7 (3.0)
Abdominal pain	2 (0.8)

One of the important issues we wanted to evaluate in our present study was whether the recreational group members were really different from those of the ED group. Interestingly, we found that the recreational users had a significantly higher level of satisfaction associated with their sexual performance. Although this appears strange, it could be associated with a better level of satisfaction due to stronger and long lasting erection.

An important point to note in our present study is the feasibility of acquiring PDE5i without a medical prescription amongst all recreational users. This appears to imply lack of control and patient education. Meanwhile, it may indicate the necessity to enact strict laws and ensure continuous supervision of the drug market.

The strengths of our present study include: (a) The use of an anonymous internet-based survey to decrease social desirability bias; (b) The recruitment of a diverse large sample of men; and (c) Assessment of the three types of ED medications that are approved by the USA Food and Drug Administration (FDA).

We think the reason for the high recreational use of the PDE5i in our present study compared with other published studies is multifactorial. PDE5i in most Middle Eastern countries are available 'over the counter' and a medical prescription is not essential to purchase it from any drug store. Another major factor that could facilitate the recreational use of PDE5i in our present study cohort is its relatively low cost and the generally good economic status of the general population in Saudi Arabia.

Nevertheless, the present study has many limitations: (a) The method of data collection via the internet by only internet users may not proportionally represent the whole targeted population; (b) It is difficult to determine whether the questions are understood and interpreted in the same way by different respondents; (c) The response rate and criteria of respondents could not be accurately evaluated due to the nature of survey and method of survey distribution. These factors may affect the validity of the data and furthermore the results of the study. Moreover, the cross-sectional nature of the survey prevents allocating a causal relation; therefore a further prospective study is warranted in order to establish such a relationship.

Conclusion

PDE5i are frequently used by the Saudi male population and most of them appear to take it as a recreational drug. Most of the users consumed PDE5i without medical prescription and reported benefits from it, even if used recreationally, which may lead to misuse and a public health problem. Further studies with appropriate sampling and data collection methods are warranted to evaluate PDE5i use, misuse, and potential risks related to its long-term abuse.

Conflicts of interest

None.

Source of funding

None.

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