Indian Journal of Pharmacy and Pharmacology 2021;8(4):280–283

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Pharmacy and Pharmacology

Journal homepage: https://www.ijpp.org.in/

Original Research Article

Evaluation of prescribing pattern of phosphodiesterase-5 inhibitors and assessing effectiveness of sildenafil and tadalafil in patients with erectile dysfunction

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ARTICLE INFO

Article history:
Received 31-03-2021
Accepted 28-09-2021
Available online 05-01-2022

Keywords:
Erectile dysfunction
PDE5 inhibitors
Sildenafil
Tadalafil
Dapoxetine and IIEF

ABSTRACT

Background and Objectives: Several factors may affect identification and treatment of erectile dysfunction by health care providers, this study evaluates prescribing pattern of PDE-5 inhibitors and assess effectiveness of Sildenafil and Tadalafil in patients with erectile dysfunction.
Materials and Methods: This is a descriptive and observational study, observed participants without providing any interventions, after fulfilling inclusion and exclusion criteria, patients were enrolled into study and informed written consent was obtained from all patients, data was obtained from medical records, analysed descriptively. International Index of Erectile Function (IIEF) Questionnaire is used in assessment of erectile dysfunction and treatment outcomes.
Results: In our study, 80% of patients were prescribed with phosphodiesterase inhibitors and 20% received nutritional supplements. 80 percent of drugs were prescribed under generic name, subjects treated with Sildenafil/Tadalafil were found to be associated with higher mean scores for questions of International Index of Erectile Function (IIEF). Tadalafil scored high in terms of sexual desire domain.
Conclusion: PDE5 inhibitors represent major first-line oral therapy option for men with erectile dysfunction, shift of market from brand to generic products allows more freedom of choice, although multiple reports suggest general equivalency of four major PDE5 inhibitors, tadalafil suggested to be preferable.

1. Introduction

Erectile dysfunction (ED), broadly defined as inability to achieve or maintain an erection sufficient for sexual intercourse[1] and has significant impact on quality of life in both physical and psychological dimensions, partners of men with ED may experience more poor quality of life than those partners who do not have ED.[2–4] ED is also marker for cardiovascular disease and correlated with general male health status regardless of etiology.[5] Compounding significant prevalence of ED and reduced quality of life, studies suggested that men often under-report because of embarrassment or lack of awareness.[6] Therefore, optimal non-pharmacologic and pharmacologic treatment for ED is necessary.

During a normal penile erection, parasympathetic stimulation leads to nitric oxide (NO) release from endothelial cells which contributes to conversion of guanosine triphosphate to cyclic guanosine monophosphate (cGMP), this decreases intracellular calcium, leading to smooth-muscle relaxation. Once relaxed, smooth muscles collapse veins, which cause reduced drainage of arterial blood, thus sustaining an erection. Given complexity of this process, multiple etiologies may contribute to inability to attain or maintain penile erection. Etiology of erectile dysfunction is classified as psychogenic, organic or mixed,

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https://doi.org/10.18231/j.ijpp.2021.050

with mixed etiology most common type.[7]

One of mainstays of erectile dysfunction treatment is oral phosphodiesterase type 5 (PDE5) inhibitor class, four major PDE5 inhibitors are sildenafil, tadalafil, vardenafil, and avanafil. During penile erection process, cGMP is metabolized through PDE5 enzyme and cannot exert its downstream effects. PDE5 inhibitors are selective and reversible, decrease cGMP metabolism leading to attainment and maintenance of erection.[8] Nonselective PDE inhibitors were used prior to discovery of link between NO and PDEs. Since then, a number of selective PDE inhibitors have been approved to treat erectile dysfunction[9] Sildenafil was first studied in clinical trials for coronary heart disease in 1991, but serendipitously had favorable effects on penile erections. By 1998, Viagra was FDA-approved as first oral treatment for erectile dysfunction.[10] Based on 2007 American Urological Association Update for Management of Erectile Dysfunction, first-line standard management includes identifying and treating organic comorbidities and psychogenic dysfunction. Oral PDE5 inhibitors remain a first-line pharmacologic treatment.[11,12]

A number of trials have examined efficacy and safety of PDE5 inhibitors with regard to objective efficacy parameters and subjective patient-preference parameters. Factors associated with improved long-term treatment include enhanced patient-provider communication, increased knowledge of drug characteristics, and optimal prescribing patterns.[13] Several studies evaluated patients' general preference for, adherence to, and satisfaction with a certain PDE5 inhibitor. A comparison of preference studies conducted on sildenafil, vardenafil, and tadalafil, found high degree of bias and flawed methodology in studies.[14] One of preferential factors may be that, tadalafil may be taken with fatty foods without disrupting bioavailability; longer duration of action and more spontaneity surrounding sexual activity may play into slight preference for tadalafil.[15]

The most commonly reported Adverse Effects for oral PDE5 inhibitors are headache, flushing, dyspepsia, dizziness, and rhinitis. Oral PDE5 inhibitors have slight off-site binding affinity to other PDE enzymes. Vasodilation and cardiovascular safety are pertinent concerns that are reflected in the drugs' contraindications, warnings, and precautions. Any concurrent use of organic nitrates is contraindicated.[16] Evaluation of drug prescription pattern is an important aspect of patient care, which also serves as a measure of the quality of care provided. A recent systematic analysis has ascertained that prescribing quality is a dimension requiring constant evaluation.[17] Satisfaction with sexual experience is considered important when evaluating impact of treatments for erectile dysfunction, yet enhanced satisfaction has been infrequently assessed in sexual trials.

This study evaluates prescribing pattern of PDE-5 inhibitors and efficacy of Sildenafil vs tadalafil in patients with erectile dysfunction.

2. Materials and Methods

Study was undertaken in collaboration with department of General Medicine in a tertiary care, conducted for a period of 3 months. Institutional ethical committee clearance was taken. This is a descriptive and observational study where participants were observed without providing any interventions related to treatment prescribed and then results are presented descriptively. After fulfilling the inclusion and exclusion criteria, patients were enrolled into study and informed written consent was obtained from all patients after a detailed explanation prior to enrolment. A total of 100 patients were enrolled into study, patients ranging from 30 to 60 years are included in the study, and patient identification details were kept confidential. Patients who had myocardial infarction, stroke, or arrhythmias in last 6 months; resting hypotension (blood pressure [BP] <90/50 mmHg) or hypertension (BP >170/100 mmHg); and unstable angina or congestive heart failure were excluded from the study

The following data were collected from patients like age and marital status, other comorbidities and prescription details like number of drugs, names of individual drugs (generic/brand), any Fixed Dose Combination (FDC) prescribed, dose, dosage form, dosing schedule, and duration of treatment and non-pharmacological methods advised. International Index of Erectile Function (IIEF) Questionnaire is used in assessment of erectile dysfunction and treatment outcomes. A score of 0-5 is awarded to each of the 15 questions that examine 4 main domains of male sexual function: erectile function, orgasmic function, sexual desire and intercourse satisfaction[18]

3. Results

In our study, 80 patients were above 40 years and 20 patients were below 40 years, mixed organic and psychogenic erectile dysfunction was much more common above 40 years and psychogenic erectile dysfunction was common below 40 years. The most common comorbid disorders identified were hypertension, diabetes and benign prostatic hyperplasia. Our study showed that odds of having erectile dysfunction increased with addiction especially cigarette smoking. Out of 100 patients, 80 patients were smokers. Hence, measures for deaddiction of smoking will play a very important role. 80 patients were prescribed with phosphodiesterase inhibitors and out of 80, 40 received Sildenafil and 40 received Tadalafil, fixed dose combination of Sildenafil+Dapoxetine were prescribed in 20 patients, Tadalafil+Dapoxetine were prescribed in 20 patients, nutritional supplements like ginseng or fenugreek extract were prescribed in 20 patients. 80 percent of drugs were prescribed under generic name. In this study subjects treated

with 100 mg oral dose of Sildenafil / 20 mg Tadalafil were found to be associated with higher mean scores for questions of International Index of Erectile Function (IIEF). Tadalafil group showed considerably greater positive responses than sildenafil group but within same significant levels. Sexual-desire domain in sildenafil treated men with respect to their aged matched controls showed a non-significant difference, where as this difference was found to be highly significant in tadalafil treated group. Frequency of penetration and maintenance of erection after sexual penetration or during masturbation were found to be enhanced significantly in both sildenafil/tadalafil treated men. Similarly mean domain of erectile function, orgasmic function, and intercourse satisfaction also showed significant improvement in both treated groups in comparison with their age matched untreated controls.

Table 1: International index of erectile function patient questionnaire

Q1	How often were you able to get an erection during sexual activity?
Q2	When you had erections with sexual stimulation, how often were your erections hard enough for penetration?
Q3	When you attempted intercourse, how often weIre you able to penetrate (enter) your partner?
Q4	During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
Q5	During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
Q6	How many times have you attempted sexual intercourse?
Q7	When you attempted sexual intercourse, how often was it satisfactory for you?
Q8	How much have you enjoyed sexual intercourse?
Q9	When you had sexual stimulation or intercourse, how often did you ejaculate?
Q10	When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?
Q11	How often have you felt sexual desire?
Q12	How would you rate your level of sexual desire?
Q13	How satisfied have you been with your overall sex life?
Q14	How satisfied have you been with your sexual relationship with your partner?
Q15	How do you rate your confidence that you could get and keep an erection?

Table 2: International index of erectile function scoring for each domain

Function domain	Maximum score
A. Erectile function (Q.1,2,3,4,5,15)	30
B. Orgasmic function (Q.9,10)	10
C. Sexual desire (Q.11,12)	10
D. Intercourse satisfaction (Q.6,7,8)	15
E. Overall satisfaction (Q.13,14)	10

4. Discussion

Choice of oral PDE5 inhibitor therapy should be guided by discussion between patient and provider that focus on understanding various characteristics, which can increase likelihood of satisfaction. Prevalence and health implications of erectile dysfunction are far-reaching. Based on shift in oral PDE5 inhibitor market from brand to generic products, patients and providers will have more freedom of choice and cost will be a lesser consideration.

IIEF (International Index of Erectile Function scoring) assessment is limited by superficial assessment of psychosexual background and partner relationship therefore to be viewed as adjunct to detailed sexual history and examination. Findings of this study suggest that both sildenafil and tadalafil may assist an individual in enhancing excitement phase or prolonging sexual interaction, further conclude that there is a major point of difference between short-acting agent sildenafil and longer acting tadalafil. This probably allows more choice about onset of sexual responses with tadalafil than with sildenafil.

5. Conclusion

PDE5 inhibitors represent a major first-line oral therapy option for men with erectile dysfunction. Although multiple reports suggest general equivalency of efficacy and safety between four major PDE5 inhibitors, tadalafil has been suggested to be preferable.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Byndoor Y, Sagar TV, Kumar S. Evaluation of prescribing pattern of phosphodiesterase-5 inhibitors and assessing effectiveness of sildenafil and tadalafil in patients with erectile dysfunction. *Indian J Pharm Pharmacol* 2021;8(4):280-283.