

## Outcome of On-Demand Tadalafil in Premature Ejaculation

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### ABSTRACT

**Background:** One of the most prevalent sexual diseases among men is premature ejaculation (PE). Phosphodiesterase type-5 (PDE5) inhibitors used on-demand were successful in treating PE, according to several studies.

**Aims:** To evaluate the safety and the efficacy of tadalafil in treatment of patients with premature ejaculation.

**Patients and methods:** This study was conducted on 30 patients with at least a 3-month history of PE. All patients were submitted to clinical examination with stress on genital examination, laboratory testing for complete blood picture, and hormonal profile. Patients were received on-demand 20 mg tadalafil 2 hours before intercourse. Intravaginal ejaculatory latency time (IELT) was measured in all patients before and after the treatment (at 4, 8, and 12 weeks).

**Results:** The mean age was  $33.03 \pm 7.5$  years, with mean body mass index (BMI) of  $28.8 \pm 2.9$  kg/m<sup>2</sup>. The baseline IELT score was  $39.4 \pm 10$ . There was highly statistically significant (**p-value < 0.001**) increased 4 weeks IELT score ( $186.6 \pm 24.4$ ), 8 weeks IELT score ( $188.5 \pm 21$ ) and 12 weeks IELT score ( $187.2 \pm 20.5$ ) when compared with baseline IELT score ( $39.4 \pm 10$ ). **Conclusion:** Tadalafil 20 mg on demand is thought to help PE patients with good levels of safety and tolerability.

**Keywords:** Tadalafil, Premature ejaculation, IELT score.

### INTRODUCTION

A male sexual disease known as premature ejaculation (PE) is distinguished by the inability to control or delay ejaculation and a short intravaginal ejaculatory latency time (IELT), and unfavourable personal effects. PE causes psychological pressure on both men and their spouses, having a significant negative impact on the marriage <sup>(1)</sup>. The preferred medications for treating PE over the past 20 years have changed from psychotherapy to medications, mainly phosphodiesterase type-5 (PDE5) inhibitors and selective serotonin reuptake inhibitors (SSRIs) <sup>(2)</sup>.

The only pharmaceutical approved to treat PE, additional off-label medications, such as long-acting selective serotonin reuptake inhibitors, or dapoxetine on demand (OD) (SSRIs), topical anaesthetics (TAs), and phosphodiesterase type 5 inhibitors (PED5is), and tramadol are the most popular therapeutic strategies for PE management <sup>(3)</sup>.

Dapoxetine on demand therapy for PE has been approved in Europe per The European Association of Urology's suggestions. Lifelong and acquired PE may both benefit with dapoxetine <sup>(4)</sup>.

The effectiveness of PDE5i in the management of PE has been supported by numerous researches. Central and peripheral responses are a few of the mechanisms that have been proposed for PDE5i's involvement in PE treatment <sup>(5)</sup>. The vas deferens, seminal vesicle, and prostate smooth muscles, and urethra could be mostly relaxed by PDE5i. Other possible outcomes include lengthening erections, decreasing sympathetic tone in the central nervous system, and more, and raising overall

intercourse enjoyment. In PE patients, using dapoxetine and PDE5i together is therefore associated with greater efficacy <sup>(6)</sup>. The study's objectives are to evaluate the efficacy and safety of tadalafil in treating patients with premature ejaculation.

### MATERIAL AND METHODS

This study was an observational prospective study done on thirty patients having at least a 3-month history of PE.

PE is characterised by (1) ejaculation that always or almost always happens prior to or within 1 minute of vaginal penetration, either present from the first sexual experience or following a new unpleasant shift in ejaculatory latency, according to the International Society for Sexual Medicine (ISSM). Patients were given a PE diagnosis if they fulfilled these criteria (2) Being unable to delay ejaculation throughout all or nearly all vaginal penetrations (3) Bad psychological outcomes, such as avoidance of sexual activity or feelings of worry, irritation, or dissatisfaction <sup>(2)</sup>. All patients received on-demand 20 mg tadalafil two hours before to sexual activity.

**Setting:** Outpatient Clinic of Urology Department, Qena University Hospital.

**Inclusion criteria:** All married patients verified as having at least a 3-month history of PE and aged older than 18 years.

**Exclusion criteria:** Patients with diabetes mellitus (DM), chronic prostatitis, patients with erectile dysfunction

(ED), or patients enrolled in the study who took PE medication within the three months before to enrolment.

**All patients were subjected to the following:**

**History and Clinical Examination:** Complete history taking from the patient, which included history of smoking status, symptoms of urological or genital disease, with the onset, course, and duration of the presenting symptoms, and other comorbid conditions. Full clinical examination: included assessment of general condition with stress on genital examination. Parameters for anthropometry were acquired. Height and weight were recorded, and body mass index (BMI), which is the product of weight in kilogrammes divided by height in metres squared, was computed.

**Laboratory Investigations:** Blood samples were collected from patients and submitted to the following: complete blood count (CBC) which included platelet count, white blood cell (WBC), red blood cell (RBC), and haemoglobin percentages (Hb%). blood glucose level after fasting. The lipid profile's components of total cholesterol (TC), very low-density lipoprotein (VLDL), and low-density lipoprotein (LDL) and triglycerides (TG). The total levels of prolactin, luteinizing hormone (LH), follicular stimulating hormone (FSH), estradiol (E2), and testosterone were included in the hormonal profile.

**Measuring Outcome:** Intravaginal ejaculatory latency time (IELT) was measured in all patients before and after the treatment using stopwatch, after explaining the ILET measurement process (beginning from the time of intromission until ejaculation).

**Ethical Approval:** The study was approved by the Ethics Board of the South Valley University and an informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Statistical analysis:** Statistical package for the social sciences (SPSS) version 26.0, was used to analyse the data. Qualitative information was given as frequency and percentage (%) and quantitative data were presented as mean and standard deviation (SD). It was deemed significant at P 0.05.

**RESULTS**

The mean age was 33.03 ± 7.5 years, with mean BMI of 28.8 ± 2.9 kg/m<sup>2</sup>, there were 15 smokers (50%). The means of baseline FBS, cholesterol, TG, HDL, LH, FSH, E2, testosterone, and prolactin are shown in table (1).

**Table 1: Demographic data, lipid profile and hormonal profile of studied patients at baseline**

Variable	Studied patients (n=30)
Age (mean± SD)	33.03± 7.5
BMI (kg/m <sup>2</sup> )	28.8± 2.9
Smoking (N%)	15 (50%)
FBS (mg/dl)	87.1 ± 7.4
Cholesterol (mg/dl)	163.2 ± 33.5
TG (mg/dl)	107.9 ± 3.8
HDL (mg/dl)	48.3 ± 9.7
LH (mIU/ml)	5.4 ± 1.2
FSH (mIU/ml)	5.3 ± 1.4
E2 (pg/ml)	33.3 ± 8.3
Testosterone (ng/ml)	664.0 ± 76.2
Prolactin (ng/ml)	6.6 ± 1.1

*TG (Triglycerides, HDL (high density lipoprotein, LH (lutinizing hormone), FSH (follicular stimulating hormone, E2 (estrogen)*

There was highly statistical significant improvement in IELT score after 4 weeks, 8 weeks, and 12 weeks when compared with baseline IELT score as in table (2).

**Table (2): IELT score in minutes at baseline and follow up at 4, 8 and 12 weeks (n=30)**

	Baseline	At 4 weeks	At 8 weeks	At 12 weeks	F value	P Value
IELT score	Mean 39.4	18.6	18.5	187.2	422.6	< 0.001
	±SD 10.0	24.4	21.0	20.5		

The most frequent side effects were headache, flushing, dizziness and nausea. There was no discontinuation of treatment owing to adverse effects (AEs) as in table (3).

**Table (3): Reported side effects in our patients**

Variable	N (%)
Headache	10 (33.3%)
Flushing	9 (30%)
Palpitation	2 (6.7%)
Dizziness	7 (23.3%)
Nausea	9 (30%)
Vomiting	5 (16.7%)
Fatigue	5 (16.7%)
Discontinuations due to AEs	0 (0%)

**DISCUSSION**

The findings of this study demonstrated statistically significant improvements in IELT scores after 4, 8 and 12 weeks of tadalafil. Mean IELT scores indicated statistically significant improvement from baseline.

This was in concordance with Şentürk *et al.* (7) who investigated 60 individuals with premature ejaculation using IELT and IIEF. Patients were supplied 5 mg tadalafil. Before the therapy, the mean IELT score was

1.49 minutes and the mean IIEFF score was 20.87. Following the treatment, both metrics showed statistically significant improvements ( $p < 0.001$ ).

100 PE patients were enrolled in a single-blind, clinical trial using a placebo and random selection between two teams (50 patients each). For six weeks, those in Group 1 were given a placebo in the form of a pill of an oral multivitamin. Group 2 received tadalafil 5 mg once daily for six weeks. The average answers to the seven questions on the AIPE questionnaire and the tadalafil test's total scores group were considerably higher than those of the placebo group following treatment. The author claims that once-daily 5 mg tadalafil therapy for PE patients for 6 weeks was successful and well tolerated (8).

In another study, a significant number of patients experienced a reduction in sexual function changes, such as early ejaculation, after using tadalafil for six months (9). This conclusion was supported by **Ozcan et al.** (10) who found that administering 5 mg of tadalafil orally once per day for a month helped persons with lifelong PE by improving their IELT and premature ejaculation traits.

**Karabakan et al.** (11) discovered that after getting treatment with 5 mg of tadalafil once day for three months, patients with ED and PE showed a significant improvement in their IELT and IIEF-5 readings. In a similar vein, administering 50 mg of sildenafil citrate on-demand for six months to PE patients one hour prior to scheduled sexual activity led to considerably greater IELT and intercourse satisfaction levels (12). Similar results were seen in men with lifetime PE who took 10 mg of vardenafil on-demand for 16 weeks. They saw a notable increase in IELT and a decrease in postejaculatory refractory time. The sensation of ejaculatory control, sexual pleasure, and self-confidence all improved (5).

Our findings demonstrated that on demand 20 mg tadalafil was well tolerated. The most common side effects were headache (33.3%), hot flashes (30%), dizziness (23.3%) and nausea (30%). There were no treatment discontinuations of therapy owing to AEs.

According to **Abu El-Hamd** (8) who found similar results to ours, tadalafil 5 mg once daily for 6 weeks was well tolerated when used to treat PE patients. Headache, back discomfort, myalgia, dyspepsia, and flushing were the predominant adverse reactions. This outcome was consistent with that of **Ozcan et al.** (10) who showed the safety of administering 5 mg of tadalafil once day for a month to the most typical adverse effects were headache, back pain, myalgia, dyspepsia, and gastric reflux in patients with longstanding PE.

## CONCLUSION

According to the findings of this research, using on demand 20 mg tadalafil as a therapy for PE patients is thought to have successful effects with a high degree of safety and tolerability.

## DECLARATIONS

- **Consent for publication:** I confirm that all authors accept the manuscript for submission
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of interest:** The authors declare no conflicts of interest regarding the publication of this paper.

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