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Research Article

A Prospective Randomized Study Comparing the Efficacy and Safety of Sildenafil with Dapoxetine in the Treatment of Premature Ejaculation

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Abstract

Introduction: Premature ejaculation (PE) is one of the most common male sexual disorders and has been estimated to occur in 20% to 40% of men. Selective serotonin reuptake inhibitors (SSRIs) are common drugs that are used in the treatment of PE. Nevertheless, the use of sildenafil combined with dapoxetine to improve its efficacy is not yet fully investigated.

Objectives: To evaluate the role of sildenafil with dapoxetine in treatment of premature ejaculation (PE).

Methods: 80 potent PE patients, divided into two equal groups; group I has given dapoxetine 30 mg 1 to 3 hr before planned sexual intercourse, and group II has given dapoxetine 30 mg 1 to 3 hr with sildenafil 50 mg 1.5 hr before planned sexual intercourse. Patients were followed up at 1 and 3 months of treatment by intra-vaginal ejaculatory latency time (IELT), grade of PE, and sexual satisfaction scale (SSS).

Results: There was a statistically significant improvement in IELT among group II patients than group I at 1 month of treatment and after 3 months. The statistical comparison showed significant improvement in IELT among group II patients at 1 month and 3 months after treatment. There was a significant reduction of a grade of PE among patients of group II than group I at baseline, 1 and 3 months of treatment respectively. There were no statistically significant differences between the two groups in side effects.

Conclusion: Sildenafil combined with dapoxetine is better than dapoxetine alone in the treatment of PE; with more tolerable side effects.

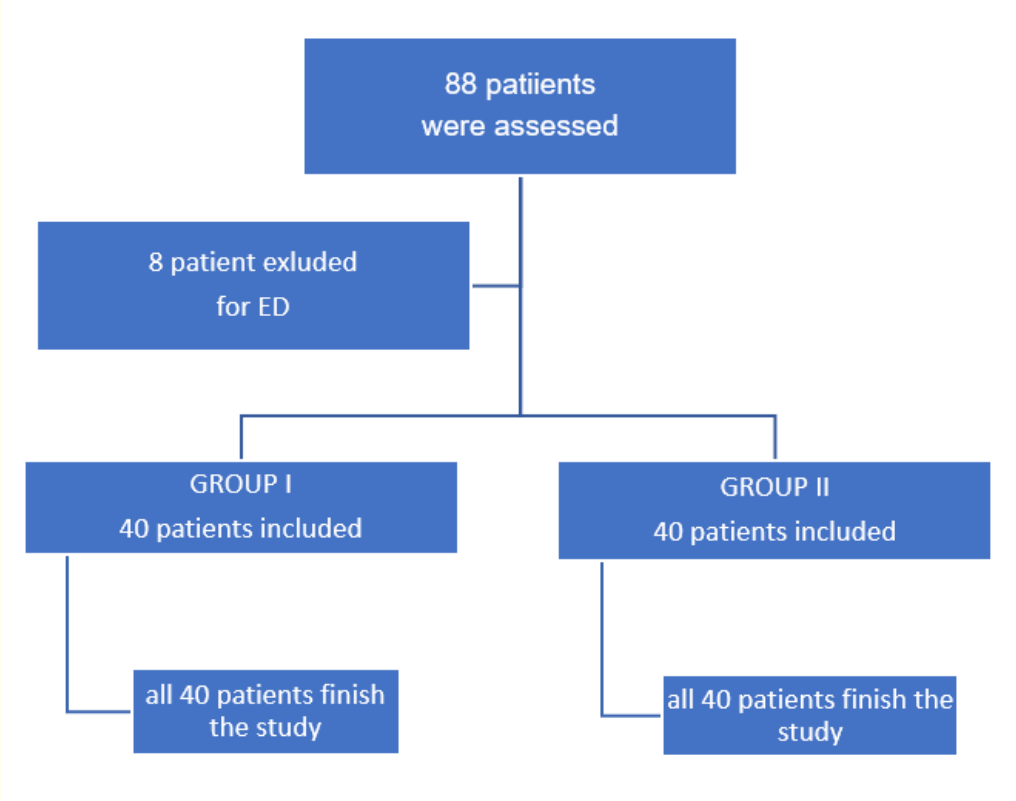
Keywords: *Dapoxetine; Male Sexual Dysfunction; Premature Ejaculation; Sildenafil*

Introduction

Premature ejaculation (PE) is the most common sexual dysfunction that occurs in 20 - 40% of men [1]. It causes negative psychological problems, such as distress, frustration, or the avoidance of sexual act. PE may be defined as primary when it occurs from the start of sexual life or secondary when it occurs after a period of satisfactory coital relationship [1,2]. Premature ejaculation might be situational with a specific partner. Acquired PE may be due to erectile dysfunction or prostatitis, also endocrine causes have been reported as a cause of PE in 50% of men with hyperthyroidism and 7.1% in hypothyroidism [3,4]. Over the past century, premature ejaculation was considered a psychological disorder that was treated through counseling and behavioral sex therapy. Premature ejaculation can be treated pharmacologically with medications that act either centrally or locally to enhance the psycho-neurological control of ejaculation and delay orgasm. Drugs for the treatment of PE include selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, tramadol, and topical agents [5,6]. Dapoxetine is the only approved drug for PE. Its efficacy and safety are well investigated [7]. Nevertheless, the use of sildenafil combined with dapoxetine to improve its efficacy is not yet fully investigated.

Materials and Methods

This is a prospective randomized study with 88 cases of PE that have been selected from outpatient clinic, from May 2020 to February 2021. Informed consent was obtained from all participants in this research with all possible side effects. All patients were potent men in a stable frequent sexual relationship for at least 6 months and had an uncontrolled ejaculation within 1 - 2 min of vaginal intromission, with no obvious organic cause. Exclusion criteria were Organic cause of PE, contraindications, or drug interaction for dapoxetine or sildenafil. Low libido, chronic depression, psychiatric illness, alcohol or drug abuse were excluded. A detailed history was taken including medical and surgical history, complete physical examination was performed, and assessment of domain A of the international index of erectile function (IIEF) to exclude patients with erectile dysfunction (ED), self-assessment of intravaginal ejaculation latency time (IELT) by stopwatch, grade of PE and sexual satisfaction scale (SSS) were recorded as a baseline data before the start of medical treatment. Eight patients were excluded before starting because of suspected ED problems. Patients were divided into two equal groups by block randomization. Group I patients were given on-demand dapoxetine 30 mg 1 - 3 hours before the planned sexual intercourse while group II patients were given on-demand dapoxetine 30 mg and demand sildenafil 50 mg 1 - 3 hours and 60 - 90 minutes before planned sexual intercourse respectively. The duration of the regimen was three months. Patients followed up at 1 month and 3 months of treatment by the IELT, grade of PE, SSS, and any side effects were recorded.



Flow diagram

Statistical analysis: Data were analyzed using IBM SPSS software package version 20.0. Comparison between different groups regarding categorical variables was tested using the Chi-square test. For normally distributed data, comparison between the two studied groups was done using independent t-test and Paired t-test for paired data, while for abnormally distributed data, a comparison was done using Mann Whitney test and Wilcoxon signed ranks test for paired data. The significance of the obtained results was judged at the 5% level.

Results

Age of patients and smoking showed no statistically significant difference between the two groups. Also, duration of illness (DOI) and frequency of intercourse per week showed no statistically significant difference between the two groups. The domain A of IIEF ranged from 22 to 28 (mean 23.78 ± 1.70) in group I and from 22 to 29 (mean 24.35 ± 1.75) in group II with no statistically significant differences between the two groups (p = 0.140).

In group I, The IELT improved from a mean of 51.72 seconds before treatment to a mean of 289 seconds and 322 seconds after 3 months of treatment. In group II, The IELT improved from a mean of 56.60 seconds before treatment to a mean of 298.75 seconds and 352.50 seconds after 3 months of treatment. Statistical comparison in the IELT between the two groups pretreatment showed no significant differences between the two groups (p = 0.067(. Statistical comparison between the IELT in either group after 1 and 3 months showed significant improvement (p < 0.001). Statistical comparison in the IELT between the two groups after 1 month of treatment showed significant improvement in group II (Median 300.0) in relation to the group I (Median 280.0) with (p = 0.039). Statistical comparison in the IELT between the two groups after 3 months of treatment showed significant improvement in group II (Median 355.0) in relation to the group I (Median 320.0) with (P < 0.001) (Figure 1).

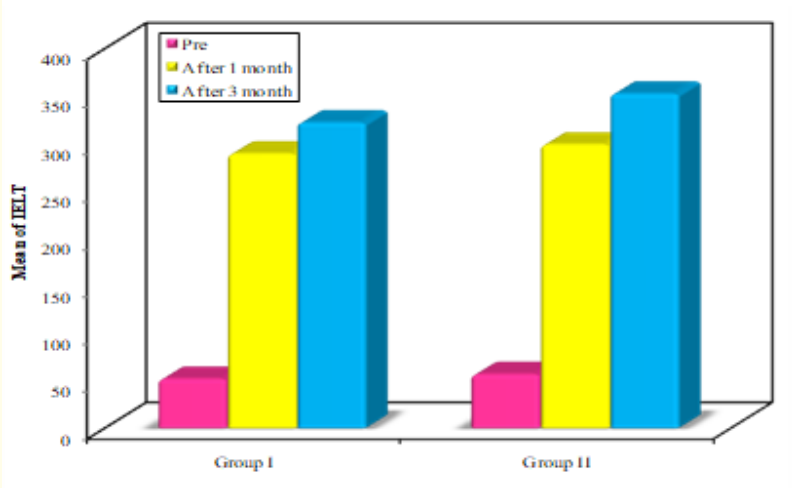


Figure 1: *Comparison between two studied groups according to IELT.*

At baseline, 1 and 3 months of treatment, the mean of SSS scores was 1.50 ± 0.60, 2.80 ± 0.65, and 3.48 ± 0.55 in group I and 1.63 ± 0.54, 3.25 ± 0.67 and 4.10 ± 0.50 in group II respectively. The statistical comparison showed significant improvement among group II patients at 1 month (P-value = 0.004) and 3 months (P-value < 0.001) of treatment (Table 1).

SSS	Pre (n = 40)	After 1 month (n = 40)	After 3 month (n = 40)	Frp
Group I				
Min. - Max.	1.0 - 3.0	2.0 - 4.0	2.0 - 4.0	< 0.001*
Mean ± SD	1.50 ± 0.60	2.80 ± 0.65	3.48 ± 0.55	
Median	1.0	3.0	3.50	
Sig.bet. periods	p1 < 0.001*, p2 < 0.001*, p3 < 0.001*			
Group II				
Min. - Max.	1.0 - 3.0	2.0 - 4.0	3.0 - 5.0	< 0.001*
Mean ± SD	1.63 ± 0.54	3.25 ± 0.67	4.10 ± 0.50	
Median	2.0	3.0	4.0	
Sig.bet. periods	p1 < 0.001*, p2 < 0.001*, p3 < 0.001*			
MWp	0.252	0.004*	< 0.001*	

Table 1: *Comparison between two studied groups according to SSS.*

For the grade of PE, there was a significant reduction in grade of PE among patients of group II than those of group I after 1 (P-value = 0.001) and 3 months (P-value = 0.004) with mean values 5.0 ± 0.82, 4.0 ± 1.11 and 3.30 ± 1.24 in group I and 4.80 ± 0.72, 3.15 ± 1.0 and 2.55 ± 0.90 in group II at baseline, 1 and 3 months of treatment respectively (Table 2).

PE grade	Pre (n = 40)	After 1 month (n = 40)	After 3 months (n = 40)	^{Fr}p
Group I				
Min. - Max.	4.0 - 8.0	2.0 - 6.0	2.0 - 6.0	< 0.001*
Mean ± SD	5.0 ± 0.82	4.0 ± 1.11	3.30 ± 1.24	
Median	5.0	4.0	4.0	
Sig.bet. periods	p1 < 0.001*, p2 < 0.001*, p3 = 0.004*			
Group II				
Min. - Max.	4.0 - 6.0	2.0 - 4.0	2.0 - 4.0	< 0.001*
Mean ± SD	4.80 ± 0.72	3.15 ± 1.0	2.55 ± 0.90	
Median	5.0	4.0	2.0	
Sig.bet. periods	p1 < 0.001*, p2 < 0.001*, p3 = 0.005*			
^{MW}p	0.301	0.001*	0.004*	

Table 2: *Comparison between two studied groups according to the grade of PE.*

^{Fr}p: value for Friedman test for comparing between the different periods.

^{MW}p: value for Mann Whitney test for comparing between the two studied groups.

p_1: p-value for Wilcoxon signed ranks test for comparing between pre and after 1 month.

p_2: p-value for Wilcoxon signed ranks test for comparing between pre and after 3 months.

p_3: p-value for Wilcoxon signed ranks test for comparing between after 1 month and after 3 months.

**: Statistically significant at p ≤ 0.05.*

As regards to the side effects; headache (2.5%), nausea (5%), dizziness (2.5%), fatigue (2.5%) and constipation (2.5%) were reported among patients of group I, while headache (7.5%), nausea (10%), nasal congestion (2.5%), flushing (2.5%), dizziness (2.5%), fatigue (2.5%) and constipation (2.5%) were reported among patients of group II. There were no statistically significant differences between the 2 groups according to the side effects (Figure 2).

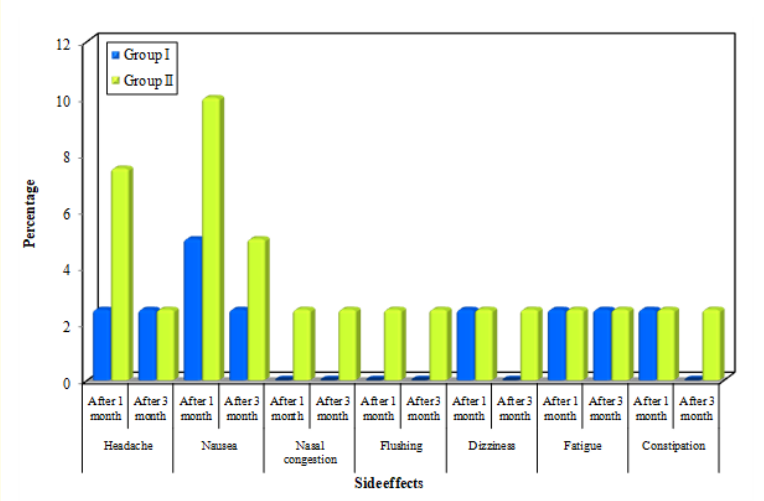


Figure 2: *Comparison between two studied groups according to side effects.*

Discussion

Pharmacological treatment of PE includes selective serotonin reuptake inhibitors (SSRIs), phosphodiesterase type-5 (PDE5) inhibitors, Tramadol, and local anesthetic ointments [8-11]. Ejaculation is affected by central serotonin (5HT) level which had an inhibitory effect on libido, orgasm, and ejaculation [12]. PDE5 inhibitors are known to be effective oral erectogenic medications. PDE5 inhibitors alter the function of smooth muscles on seminal vesicles and the vas deferens [13].

This study was conducted on 80 patients complaining of PE to find out if sildenafil had a role in the treatment of PE when it was given on-demand with dapoxetine 30 mg. Intra-vaginal ejaculatory latency time (IELT), sexual satisfaction scale (SSS) and grade of PE had been compared in both groups with significant improvement at the end of the study. This improvement was significantly higher in combination therapy. Side effects were significantly higher with combination therapy with no cases of treatment discontinuation.

New studies have discovered the role of dapoxetine in the treatment of PE; some of them showed that dapoxetine 30 mg is less effective than dapoxetine 60 mg and has fewer side effects [12,14]. Yue FG., *et al*. (2015) in a meta-analysis of 5 randomized controlled studies comparing dapoxetine with placebo reported that dapoxetine was more effective than placebo proved by significant improvement in IELT ($P < 0.001$) [15].

Sildenafil has been investigated as an adjuvant to dapoxetine in the treatment of PE; Chen., *et al*. (2003) has added 25 - 100 mg sildenafil 1h before intercourse to the regimen of patients who were not satisfied with paroxetine alone with good results regarding IELT and PE grade [13].

E. C. Polat., *et al*. (2015) in a study to evaluate the effectiveness of paroxetine and tadalafil combination in the treatment of PE reported statistically significant improvement in IELT scores at end of treatment. IELT scores have returned close to the baseline after discontinuation of treatment [16].

Lee WK., *et al*. (2013) in a prospective, randomized, double-blind, placebo-controlled and multicenter study reported that a low dose of dapoxetine combined with mirodenafil showed better results in IELT compared with dapoxetine only [17]. SSS showed significant improvement after 1 and 3 months of medical treatment. Side effects were higher with combination therapy than dapoxetine only but still tolerable by all the patients in this study. These results support the suggestion that the PDE5 inhibitors have a potential role in the treatment of PE without ED.

Kim., *et al*. (2015) in a randomized crossover study in potent male volunteers reported that concurrent usage of PDE5 inhibitors (udenafil) and SSRIs (dapoxetine) was generally well tolerated [18].

Limitations in our study include a low patient number and short follow-up time. Also, we haven't evaluated female partner intercourse satisfaction.

Conclusion

Both on-demand oral dapoxetine 30mg in combination with on-demand oral sildenafil 50mg are effective in the treatment of PE in regards to IELT, PE grade, and sexual satisfaction scale (SSS). Combination therapy showed better results regarding IELT, SSS, and grade of PE with more tolerable side effects. Further studies are needed with more fellow up period and to assess the female partner satisfaction.

Conflict of Interest

None.

Funding Source

None.

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