COMPARISON OF PAROXETINE AND DAPOXETINE IN PREMATURE EJACULATION

Sarhad Khan[1], Khalid Farooq[1], Najma Hameed[2]

ABSTRACT

Objective: To compare the efficacy of Paroxetine and Dapoxetine in premature ejaculation.
Methodology: We enrolled One hundred and twenty-six patients in this study from January 2019 to December 2021 in urology department Medical teaching institute Lady Reading hospital Peshawar by using convenient sampling technique. Patients were assigned to take either 20mg OD Paroxetine (n =158) or 30mg OD Dapoxetine(n=159). On follow-up after six weeks, all the patients were assessed for improvement in intravaginal ejaculation latency timings (IELT). T test was applied to see any significant difference in both groups assuming P value <0.005 as statistically significant.
Results: The mean age of the study population was 32.17±8.38 years. The efficacy in term of increase in the IELT more than one minutes was 82.53% in paroxetine group and 74.60% in Dapoxetine group with no statistically significant difference in both drugs *(p=0.277).* The mean IELT before starting drug was 0.56±0.30 minutes in Paroxetine group and 0.49±0.29 second in Dapoxetine group. After the treatment, in paroxetine group the timings improved to 5.31±3.27 minutes and to 4.86±3.36 minutes in dapoxetine group. T
Conclusion: Dapoxetine and Paroxetine in dose of 20mg and 30mg have equal efficacy in terms of
Increasing the intravaginal ejaculation latency time (IELT), so both are equally effective for treatment of premature ejaculation.
Keywords: Dapoxetine, Paroxetine, Premature ejaculation (PE), sexual disorder

INTRODUCTION

The International Society for Sexual medicine (ISSM) has defined Premature ejaculation (PE) as "a male sexual disorder characterized by ejaculation which always or nearly always happens before or at intervals concerning one minute of vaginal penetration; the inability to delay ejaculation on all or nearly all vaginal penetrations; and negative personal consequences, like distress, bother, frustration and/or the rejection of sexual intimacy" [1].PE is one of the most familiar male sexual disorder having prevalence rates of 20% to 40% [2-4].

1. Lady reading Hospital, Peshawar, Pakistan
2. Khyber Girls Medical college, Peshawar, Pakistan

Address for Correspondence:
Dr. Khalid Farooq
Department of Urology, Lady reading hospital, Peshawar, Pakistan
drkf846@yahoo.com
00923455908751

Premature ejaculation is classified as primary, lifelong or secondary known as acquired[5]. Lifelong PE is early ejaculation while making attempt with nearly each partner on nearly every sexual intercourse from the primary sexual encounter onward, whereas acquired PE evolves in a man's healthy sexual life at some specific time when his previous ejaculation episodes were normal and is secondary to psychological or urological pathology[5].Some andrologists additionally classify two more subgroups of PE, including natural-variable PE and premature-like ejaculatory dysfunction. Natural-variable PE is characterized by early ejaculations occurring on scattered instances and presumed to be a usual alteration in sexual performance[5]. Premature-like ejaculatory dysfunction is the fictitious belief of sexual dysfunction in spite of the fact that they enjoy lengthy time durations of love with their partners[5].

The influence of PE on both partners can be significant. The male partner develops a strong feeling of shame and embarrassment for not being in a position to satisfy and give pleasure to his partner and subsequently sense of inferiority complex low self-esteem and anxiety are the common psychological problems to emerge[6-9]. Degree of satisfaction with sexual intercourse and the sexual accord might be decreased whereas private discomfort and

misery and social challenge can also be experienced in patients with PE [7,9-11], resulting in both compromised quality of life and psychological well-being [9]. In two trials of the female partners, sexual delight was "poor" or "very poor" in nearly 25% of participants, having male partners suffered with PE. In 50% of respondent's private distress associated with PE was moderate, whereas 32% of the study participant's exhibited moderate level of inter personal challenges. [11]. The level of perceived sense of lack of self-control over ejaculation, personal misery, satisfaction with sexual intercourse, and difficulty for mutual relationship is nearly equal for men with PE and their better halves[10]. The negative impact on the quality of life of both male and their partner illustrate the need for better and systematized strategies of PE diagnosis, evaluation and treatment[2].

Therefore, the cognitive, behavioral and medical remedies are critical element for PE management. Lifelong PE is treated by medications whereas premature like ejaculatory dysfunction is mostly treated by behavioral remedies and psychotherapy. Behavioral strategies have normally centered on the physical issue of PE, together with the "squeeze" approach initially reported by Masters and Johnson in 1970 and the "stop-start" approach reported by Semen's in 1956[12]. Short-term positive results have been achieved by these cost-effective techniques; however, the data regarding the potency of these practices in the long term is scarce[13-16]. A variety of pharmaceutical solutions have been in practice for the management of PE range from topical agents that can be applied on need basis associated with a smaller number of adverse systemic consequences than oral medications. However, some of the undesired consequences of these remedies may include loss of erectile strength, burning sensation in vagina of the woman counterpart, and insensibility of the genitalia in both partners[17-19].

The aim behind behavioral cures is pleasure, control, self-belief and satisfaction. Results can be augmented when coupled with pharmacological modality [2]. Delayed ejaculation is an unfavorable effect of Selective serotonin reuptake inhibitors (SSRIs). In some men suffering from premature ejaculation, the capacity of the SSRIs to lengthen ejaculation has been remedial. Multiple trials assessing the ejaculation-delaying capability of SSRIs revealed that paroxetine, fluoxetine, sertraline, and citalopram produced a statistically widespread amplification in the ejaculation latency time in contrast with placebo. In one of the land mark trial where 344 sufferers with established psychiatric disorder treated with SSRIs, the occurrence of delayed ejaculation was 46% to 59%[20]. In another research study (N = 1022), 50% to 64% had delayed ejaculation secondary to use of SSRIs[21] The prevalence of delayed ejaculation following paroxetine was 24% as compared to 12% for fluoxetine reported by another study conducted on 203 depressed patients[22].The regular use of selective serotonin reuptake inhibitors (SSRIs) in PE management suggests that the traditional psychological view of PE is no longer justifiable as the only feasible pathogenesis of PE, and that serotonin has an important role in the ejaculation physiology[23-26]. For this reason, this study was conceived to test and compare the Dapoxitine being a recommended drug used for premature ejaculation treatment although not easily available in pharmacies against another Selective serotonin Re-uptake inhibitor (SSRI) Paroxitine freely available in pharmacies if proved equally effective it will be easy for the patients to find an effective remedy.

METHODOLOGY

We conducted this comparative study among patients visiting urology clinic at Lady Reading Hospital, Peshawar from January 2019 to December 2020 after taking Institutional review board approval (57-1/LRH-MTI). All the patients having IELT of less than 01 minute were taken as patient of PE were taken as patient of PE. The calculated sample size at 95% confidence level, 5% margin of error and considering the probability of dapoxitine being more efficient being 71% was 317[27]. Considering the study being conducted during the Covid, a total of 317 consented patients aged 21 to 50 years and screened for primary PE were enrolled in this study from outpatient department by a single urologist using convenient sampling technique. Patients already diagnosed with erectile dysfunction (ED), PE secondary to sexual abuse, mood or anxiety disorder diagnosed by a psychiatrist, chronic prostatitis, bladder out flow obstruction, psychoactive medication use, cancer and diabetes were excluded from this study. For allocation of recruited patient to both paroxetine and dapoxitine groups, odd and even number sequence generation was followed respectively. All recruited patients with primary PE were married, having single sexual partner and heterosexual. Any psychotropic medications were forbidden during study. Detail history and examination was done for all patients and IELT was estimated using

stopwatch method. PE was defined as an intra-vaginal ejaculation latency time (IELT) of less than 1 min after vaginal intercourse occurring in more than half of the occasions where as efficacy was defined as increase in IELT of more than one minute.

The patients were allocated to take 20mg OD paroxetine 3 to 4 hours before intercourse group A(n=158) or 30mgOD dapoxetine 1 to 3 hours before intercourse group B (n=159) during a 6-week period by convenient sampling method, then patients were reviewed 6 weeks after by the same urologist and were reevaluated for premature ejaculation. Approximate improvement in IELT score estimated by patient was noted by the principal author himself as per description of patients in minutes on the basis of stopwatch method. Data was collected on a structured Proforma. T-test was applied to test the difference of both drugs in terms of IELT.

RESULTS

The mean age of our participants was 32.17±8.38 years. The efficacy in term of increase in the IELT more than one minutes was 82.53% in paroxetine group and 74.60% in Dapoxetine group with no difference in both drugs (p=0.277) (table 1). The mean IELT before starting drug was 0.56±0.30 minutes in Paroxetine group and 0.49±0.29 second in Dapoxetine group. After the treatment, in paroxetine group the timings improved to 5.31±3.27 minutes and to 4.86±3.36 minutes *(p<0.05)* in dapoxetine group (table 2). The age groups also projected the same increase in groups with no statistically significant association with age *(p=0.667)* (table 3)

Table 1: Efficacy of paroxetine and Dapoxetine

Group	Efficacy		Total	P value
	Yes	No		
Paroxetine group	130 (82.53%)	28 (17.47%)	158	0.277
Dapoxetine group	118 (74.60%)	41 (25.40%)	159	
Total	248	69	317	

Table 2: IELTS before and after the treatment with paroxetine or Dapoxetine

Group		IELTS (in minutes) before treatment	IELTS (in minutes) after treatment	p-value
Paroxetine Group	Mean	0.5570	5.3125	0.000
	Std. Deviation	0.30353	3.27114	
Dapoxetine group	Mean	0.4986	4.8667	0.000
	Std. Deviation	0.29395	3.36931	
Total	N	317	317	
	Mean	0.5278	5.0896	
	Std. Deviation	0.29902	3.31484	

Table 3: Relationship of Age and Drug Efficacy in terms of IELT

				Group		p- value
				Paroxetine Group	Dapoxetine group	
				Count	Count	
Age groups	21 to 30 years	Efficacy	Yes IELT	50 5.423min	43 4.7	0.667
			No IELT	10 0.567min	14 0.471min	
	31 to 40 years	Efficacy	Yes IELT	65 5.282min	53 4.14min	0.513
			No IELT	12 0.489min	15 0.351	
	40 to 50 years	Efficacy	Yes IELT	15 4.37min	22 3.859mim	0.571
			No IELT	6 0.462min	12 0.321min	

Yes shows improvement time in IELT
No shows no improvement from baseline

DISCUSSION

In our study there was no statistically significant difference between paroxitene and dapoxitene in terms of increase in intravaginal ejaculation latency timingseven with the age group comparison. The mean age in our study was 32.17±8.38 years, similar to the study conducted by Semsik et al, having average age of all the patients as 33.1 ± 3.2 year and Fazal et al. where average age was 32±10.45[28- 29]. The study by Fazal et al showed effectiveness of Dapoxetine in 64(68%) patients whereas Placebo was effective in 35(37%) patients as compared to our results which showed a bit higher effectiveness for dapoxetine i.e. 74.6%[29]. In another study which compared both paroxetine and dapoxetine showed that the IELT improved from reference line to post-treatment by 117% ,117% and 170% in the paroxetine group (P < 0.01), 30 mg dapoxetine group (P < 0.01) and 60 mg dapoxetine group (P < 0.01), respectively. Interestingly this study is in strong agreement with us showing Paroxitene 20mg and Dapoxitene 30 mg equally effective [28].

In both groups of our study the IELT increase was from 0.49±0.29 to 5.31±3.27 minutes. Findings from another study reported paroxetine of 20mg/day increased the IELTS from 1.5 to 7 minutes which is inline to our results.[27]. This study results are also in agreement with Waldinger et al. which showed IELT increase to 10 minutes after 20-40mg dose of paroxetine after 6 weeks of treatment compared with placebo (p=0.002)[30]. A study conducted by Safri et al. showed comparing Paroxitene 20mg against Dapoxitene 60mg in 350 patients for 12 weeks and found paroxitene more effective in terms of IELT increment that is after 12-week of doses with dapoxetine, paroxetine, and placebo, the mean IELT was increased from baseline level of 38, 31 and 34 seconds to increased levels of 179, 370 and 55 seconds, respectively (*p<0.05* in both cases). This study support our results that paroxetine can be an alternative to Dapoxetine[31]. In another study average IELT before starting of medicine was 0.90 ± 0.47 minute, 0·92± 0.50 minute, and 0.91± 0.48 minute, and after 12week was 1.75± 2·21 minutes for placebo, 2·78 ± 3.48 minutes for 30 mg dapoxetine, and 3.32 ± 3.68 minutes for 60 mg dapoxetine[32]. The result of 20mg of paroxetine 3 to 4 hours before intercourse or with daily 10mg paroxetine has also increased IELT[33]. Dapoxetine (60 mg) 1–3 h before scheduled intercourse is a very potent treatment method for PE[28].Another study found that 60mg dapoxetine is of higher efficacy as compared to 30mg dose but the weak points in this study is that the study population belongs to America and Europe, that's why the results can't be applied to our population. Moreover there were different followup duration in different populations that's why the results can't be relied upon[34]. Further research may be done to compare dapoxetine 60mg and paroxetine 20 mg in our population.

Premature ejaculation is a male sexual disorder mediated by the changes in levels of 5- Hydroxy tryptamine neurotransmission. Previously the novel treatment for premature ejaculation was mono amine oxidase inhibitors and alpha-

adrenergic blocking agents. In 1994 it was Foster who first recommended Fluoxetine as a treatment of premature ejaculation and till date the adverse effect of SSRI is used as the treatment of premature ejaculation. Complementary and alternative systems of medicine like Chinese medicine acupuncture and ayvervadic has also been useful. Rapid absorption and quick elimination are the qualities which make dapoxetine a novel treatment for PE[28].

Occasionally the adverse effect of SSRI leads to its discontinuation. The most common side effect noted are GI upsets, dizziness and headache. Detrimental effects have resulted in stoppage of SSRI in 1.3%, 3.9%, and 8.2% of participants with placebo, dapoxetine 30 mg and dapoxetine 60 mg respectively[35]. Decreased libido in 42 to 64% of patients, anorgasmia in 31%–53% of patients and erectile impairment in up to 40% have been reported, following treatment with SSRIs[20, 21]. Furthermore sudden stopping of the drug can also produce discontinuation syndrome which is characterized by dizziness, GI upsets, fatigue headache or walking problem[36]. Hepatic impairment and concomitant administration with cytochrome P450 inhibitors are contra-indication for SSRI administration. Further research is going on other alternative therapeutics keeping in view addiction with SSRI and in future Tramadol, Alpha one blockers may be recommended as treatment in PE.

Being a comparative study, with reasonable sample size and no drop out till follow up contributed to the strength of the current study, where as having majority of the illiterate study participants not able to record their IELT for six weeks on regular basis was major limitation.

CONCLUSION

Based on the findings of the current study, it is concluded that dapoxetine and paroxetine in dose of 20mg and 30mg respectively have equal efficacy in terms of increase in IELT, so is equally effective for treatment of premature ejaculation, except that Dapoxitene is relatively difficult to find in local markets in Pakistan as compared to Paroxetine

CONTRIBUTORS

SK and KF conceived the idea, designed the study and wrote initial manuscript. NH helped in executing the plan after going through the study protocol, data collection, interpretation and revising the manuscript. SK, KF and NM reviewed the draft critically, carried out corrections and supervised the whole study. All authors contributed significantly to the submitted manuscript.

FUNDING

The study did not have a funding source.

CONFLICT OF INTEREST

All authors declare no potential conflicts of interest.

REFERENCES

1. McMahon CG, Althof SE, Waldinger MD, Porst H, Dean J, Sharlip ID, Adaikan PG, Becher E, Broderick GA, Buvat J, Dabees K. An evidence-based definition of lifelong premature ejaculation: report of the International Society for Sexual Medicine (ISSM) ad hoc committee for the definition of premature ejaculation. The journal of sexual medicine. 2008 Jul 1;5(7):1590-606.
2. Rastrelli G, Cipriani S, Corona G, Vignozzi L, Maggi M. Clinical characteristics of men complaining of premature ejaculation together with erectile dysfunction: a cross-sectional study. Andrology. 2019 Mar;7(2):163-71.
3. Carson C, Gunn K. Premature ejaculation: definition and prevalence. International journal of impotence research. 2006 Sep;18(1):S5-13.
4. Porst H, Montorsi F, Rosen RC, Gaynor L, Grupe S, Alexander J. The premature ejaculation prevalence and attitudes (pepa) survey: Prevalence, comorbidities, and professional help-seeking. European urology. 2007;51(3):816-824.
5. Waldinger MD. Recent advances in the classification, neurobiology and treatment of premature ejaculation. Sexual dysfunction. 29: Karger Publishers; 2008. p. 50-69.
6. Dunn KM, Croft PR, Hackett GI. Association of sexual problems with social, psychological, and physical problems in men and women: A cross sectional population survey. Journal of Epidemiology & Community Health. 1999;53(3):144-148.
7. Rowland D, Perelman M, Althof S, Barada J, McCullough A, Bull S, et al. Ejaculation disorders: Self-reported premature ejaculation and aspects of sexual functioning and satisfaction. The journal of sexual medicine. 2004;1(2):225-232.
8. Rowland DL, Patrick DL, Rothman M, Gagnon DD. The psychological burden of premature ejaculation. The Journal of urology. 2007;177(3):1065-1070.
9. Hanafy S, Hamed AM, Hilmy Samy MS. Prevalence of premature ejaculation and its impact on the quality of life: Results from a sample of Egyptian patients. Andrologia. 2019 Sep;51(8):e13298. Giuliano F, Patrick DL, Porst H, La Pera G, Kokoszka A, Merchant S, et al. Premature ejaculation: Results from a five-country european observational study. European urology. 2008;53(5):1048-1057.
10. Patrick DL, Althof SE, Pryor JL, Rosen R, Rowland DL, Ho KF, et al. Premature ejaculation: An

observational study of men and their partners. The journal of sexual medicine. 2005;2(3):358-367.
11. Semans JH. Premature ejaculation: A new approach. Southern Medical Journal. 1956;49(4):353-357.
12. Saadat SH, Ahmadi KH. The comparison of on-demand caffeine consumption with squeezing technique on treating patients with premature ejaculation; a randomized clinical trial. Pakistan Journal of Medical & Health Sciences. 2021;15(6):2005-10. De Amicis LA, Goldberg DC, LoPiccolo J, Friedman J, Davies L. Clinical follow-up of couples treated for sexual dysfunction. Archives of Sexual Behavior. 1985;14(6):467-489.
13. Hawton K, Catalan J, Martin P, Fagg J. Long-term outcome of sex therapy. Behaviour Research and Therapy. 1986;24(6):665-675.
14. McCabe MP. Evaluation of a cognitive behavior therapy program for people with sexual dysfunction. Journal of Sex &Marital Therapy. 2001;27(3):259-271.
15. Butcher MJ, Zubert T, Christiansen K, Carranza A, Pawlicki P, Seibel S. Topical agents for premature ejaculation: a review. Sexual Medicine Reviews. 2020 Jan 1;8(1):92-9.
16. Pozzi E, Belladelli F, Bebi C, Salonia A, Boeri L. Topical Treatment of Premature Ejaculation: The Rise of Anesthetic Spray Formulations?. Uro. 2021 Mar 12;1(1):30-8.
17. Montejo AL, Llorca G, Izquierdo JA, Rico-Villademoros F. Incidence or sexual dysfunction associated with antidepressant agents: A prospective multicenter study of 1022 outpatients. The Journal of clinical psychiatry. 2001.
18. Chouinard G, Saxena B, Bélanger M-C, Ravindran A, Bakish D, Beauclair L, et al. A canadian multicenter, double-blind study of paroxetine and fluoxetine in major depressive disorder. Journal of affective disorders. 1999;54(1-2):39-48.
19. Godpodinoff ML. Premature ejaculation: Clinical subgroups and etiology. Journal of sex & marital therapy. 1989;15(2):130-134.
20. Goldstein I. Premature to early ejaculation: A sampling of manuscripts regarding the most common male sexual dysfunction published in the ijir: The journal of sexual medicine. Nature Publishing Group; 2003.
21. Waldinger MD. Emerging drugs for premature ejaculation. Expert opinion on emerging drugs. 2006;11(1):99-109.
22. Williams W. Secondary premature ejaculation. Australian and New Zealand Journal of Psychiatry. 1984;18(4):333-340.
23. W Peng J, Fang D, Li H, Tang Y, Yuan Y, Cui W, Gao B, Li H, Zhang Z. Efficacy of dapoxetine treatment in Chinese patients with premature ejaculation and possible factors affecting efficacy in the real-world practice. BMC urology. 2020 Dec;20(1):1-6.
24. Simsek A, Kirecci SL, Kucuktopcu O, Ozgor F, Akbulut MF, Sarilar O, et al. Comparison of paroxetine and dapoxetine, a novel selective serotonin reuptake inhibitor in the treatment of premature ejaculation. Asian J Androl. 2014;16(5):725-727.
25. Elahi F, Uddin N, Hussain M, Amanullah A, Ali N. Comparison of effectiveness of dapoxetine vs placebo for prolonging intra vaginal ejaculatory latency time in premature ejaculation. Journal of Saidu Medical College. 2019;9(1).
26. Waldinger MD, Hengeveld MW, Zwinderman AH. Paroxetine treatment of premature ejaculation: A double-blind, randomized, placebo-controlled study. American journal of psychiatry. 1994;151(9):1377-1379.
27. Safarinejad MR. Comparison of dapoxetine versus paroxetine in patients with premature ejaculation: A double-blind, placebo-controlled, fixed-dose, randomized study. Clinical neuropharmacology. 2006;29(5):243-252.
28. Pryor JL, Althof SE, Steidle C, Rosen RC, Hellstrom WJG, Shabsigh R, et al. Efficacy and tolerability of dapoxetine in treatment of premature ejaculation: An integrated analysis of two double-blind, randomised controlled trials. The Lancet. 2006;368(9539):929-937.
29. McMAHON CG, Touma K. Treatment of premature ejaculation with paroxetine hydrochloride as needed: 2 single-blind placebo controlled crossover studies. The Journal of urology. 1999;161(6):1826-1830.
30. Du Y, Jiang Y, Zhang J, Tian G, Zhang N, Wu D, et al. Efficacy and safety of “on-demand” dapoxetine in treatment of patients with premature ejaculation: A meta-analysis. Medical Science Monitor. 2019;25:4225-4232.
31. Buvat J, Tesfaye F, Rothman M, Rivas DA, Giuliano F. Dapoxetine for the treatment of premature ejaculation: Results from a randomized, double-blind, placebo-controlled phase 3 trial in 22 countries. European Urology. 2009;55(4):957-968.
32.
lack K, Shea C, Dursun S, Kutcher S. Selective serotonin reuptake inhibitor discontinuation syndrome: Proposed diagnostic criteria. Journal of Psychiatry and Neuroscience. 2000;25(3):255