Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: www.saspublishers.com

OPEN ACCESS

Urology

Premature Ejaculation: A Comparative Study of on Demand Dapoxetine and Daily Dosing Paroxetine in Terms of Efficacy and Side Effect Profile

Barun Kumar[1], Dilip Kumar Pal[2*]

[1]PDT, MCH Urology, IPGMER & SSKM Hospital, Kolkata, West Bengal, India
[2]Professor & HOD, Department of Urology, IPGMER & SSKM Hospital, kolkata, West Bengal, India

***Corresponding author Dilip Kumar Pal**
| **Received:** 12.03.2019 | **Accepted:** 26.03.2019 | **Published:** 30.03.2019
DOI: 10.36347/sjams.2019.v07i03.062

Abstract **Original Research Article**

Premature ejaculation is the most common male sexual disorder causing psychological distress for both partners and diminished quality of life. With the advent of selective serotonin reuptake inhibitor causing delayed ejaculation and their subsequent use in treatment of premature ejaculation, it is now the cornerstone of drug therapy in premature ejaculation. In the past, both on demand and daily dosing of multiple drugs have been studied. However, their efficacy and side effect has not been studied comparatively. In our study, patients with premature ejaculation with intravaginal ejaculation latency time (IELT) of less than 60 seconds were included. Patients with known history of substance abuse were excluded. Patient and their partner were taught to measure IELT with a stopwatch. Thirty patients were given on demand 30mg dapoxetine and another thirty patients were given 20mg daily dose of paroxetine. They were called up after four weeks and increase in IELT and side effects were recorded. After 4 weeks, mean increase in IELT in the dapoxetine group was 57.06 seconds while in paroxetine group was 64.5 seconds. The mean increase in IELT was more in daily dose paroxetine was more and it was statistically significant. Side effect profile was similar in both groups with daily dosing group experiencing slightly more side effects. Nausea headache and diarrhea were the most common side effects. Anejaculation and loss of libido were rare but serious side effects. Both dapoxetine and paroxetine are effective drugs for premature ejaculation and they have been shown to increase IELT in daily or on-demand dosing. It was shown that daily dosing paroxetine was more effective than on-demand dosing of dapoxetine but with slightly more side effects. Both drugs have good tolerability.

Keywords: Duloxetine, Paroxetine, Premature ejaculation.

INTRODUCTION

Premature ejaculation is the most common male sexual disorder and it affects as many as 20-40% [1, 2] of men. Needless to say, it's a huge burden on sexual and mental health of a significant proportion of population.

International Society for Sexual Medicine has given the following definition of premature ejaculation: ''PE is a male sexual dysfunction characterized by ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration; inability to delay ejaculation on all or nearly all vaginal penetrations; and negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy [3].''

Etiology of premature ejaculation is difficult to be attributed to a single cause and a variety of factors play role in the etiopathogensis. The major factors have been cited as psychological that includes early sexual experiences, sexual conditioning, frequency of sexual intercourse and psychodynamic explanations. A biological explanation of lifelong premature ejaculation has been proposed to be hyposensitivity of the 5-HT2C and/or hypersensitivity of the 5-HT1A receptors [4]. This has been the basis of the use of selective serotonin reuptake inhibitor in the treatment of premature ejaculation which has revolutionized the pharmacological treatment of premature ejaculation. Premature ejaculation can further be classified as either primary i.e. from the beginning of sexual life or secondary including patients who earlier had a normal ejaculation time but have acquired decreased latency later. Patients with primary premature ejaculation have relatively shorter latency time and are difficult to treat. Secondary premature ejaculation is commonly associated with erectile dysfunction and most commonly have a psychosomatic etiology.

The diagnosis of premature ejaculation is largely on clinical parameters and on self-reported parameters that include following clinical criteria.

- Intravaginal ejaculatory latency time measured by female by a stopwatch. (IELT)
- Voluntary control to defer ejaculation
- Sexual satisfaction
- Distress

Out of these, IELT is the most common parameter used in the research setting. It is a reliable and reproducible method of objectifying the data. It is measured in seconds where ante-portal ejaculation i.e. during foreplay accounts to zero seconds. IELT of less than 60 seconds have been considered as 'definite' and between 60 to 90 seconds have been considered as 'probable' [5].

There is variety of methods which has been proposed and is in use for premature ejaculation. Most of them are directed towards behavioral modifications.

- Pelvic floor muscle exercise: helps in voluntary control for delay of ejaculation.
- Pause-squeeze technique: in this technique, partner squeeze the penis at the junction of body and glans when there is urge to ejaculate and maintain until the urge is passed.
- Stop- start technique : to discontinue intercourse when there is urge to ejaculate and start again when the urge is passed
- Topical anesthetics: combination of lidocaine-prilocaine either in a cream or spray formulation.
- Condoms: with either thick latex or coating with benzocaine or lidocaine.
- Drugs: most of the drugs used previously were antidepressants and mild sedatives. However most of them were not FDA approved and neither standard regimen nor a standard dosing was available.

On demand Dapoxetine

The only drug to be developed specifically for the treatment of premature ejaculation has gained rapid recognition and approval by drug controlling bodies all over the world. The major advantage of dapoxetine was the dose-proportional pharmacokinetics, which allows it to be an ideal on demand drug. Dapoxetine has a Tmax of 1.4–2.0 hours and rapidly achieves peak plasma concentration (Cmax) following oral administration. The mean half-life of dapoxetine after a single dose is 0.5–0.8 hours and plasma concentrations rapidly decline to about 5% of Cmax at 24 hours. The terminal half-life of dapoxetine was 15–19 hours after a single dose and 20–24 after multiple doses [6]. The standard dosing is 30 mg and the standard daily frequency is once per day. In case of suboptimal response, the dose can be adjusted to 60 mg.

There has been multiple animal and human trials [7-9] showing efficacy of dapoxetine over placebo with first dosing and maintained efficacy with subsequent dosing. There was significant increase in IELT in all the studies. Patient control over ejaculation was also assessed and has been shown to be significantly increased with dapoxetine. Another advantage of dapoxetine is low adverse effect profile. Nausea and headache are the most commonly reported adverse effect, rarely warranting discontinuation of medication. Other adverse effects include diarrhea, dizziness, and rarely erectile dysfunction. Incidence of drug withdrawal syndrome, which is common with chronic SSRI treatment, has been seen to be low with dapoxetine. Also it was found to be safe with patients with cardiovascular conditions including angina [10].

Daily dosing paroxetine

The use of SSRI for premature ejaculation was inspired by the reported adverse effect of delayed ejaculation in patients treated by SSRI for depression. Not long after it was realized multiple studies have reported its efficacy in treatment of premature ejaculation. Fluoxetine, sertraline, paroxetine all have been tried with reasonably good outcome for this condition. However, a group of patients fail to respond to paroxetine, especially one with lifelong premature ejaculation.

Paroxetine have been shown to have better outcome than other SSRI, more so in a once daily dosing than on-demand dosing [11]. The pharmacokinetics of paroxetine allows a single dosing and minimal drug interaction except for monoamine oxidase inhibitors which is the only contraindication for use with paroxetine. The dual mode of mechanism involves one with direct inhibition of central serotonin reuptake causing immediate changes in ejaculation time. The delayed changes are due to psychopathological changes with improvement in depression and more prominent with daily dosing. The concerning side effects reported with use of paroxetine were anejaculation and failure to experience orgasm even after ejaculation was in the rate of 5-8% [11]. The other side effects reported were nausea, headache, constipation and occasionally tremor.

MATERIALS AND METHODS

The study was conducted on patients attending outdoor with complain of premature ejaculation at a tertiary care hospital in India from 1st October to 31st December 2017. Patients with known history of substance abuse, psychiatric illness, and those on psychotropic drugs were excluded. Patients who were enrolled in the study were informed about the study and the possible side effects of the drugs. Also, patients and their partner were taught how to measure IELT using a stop watch and they were called after one week with recorded IELT of minimum three intercourse. Patients with mean IELT of more than 60 seconds were excluded. After that, patients were randomly given either on demand dapoxetine (30mg, 1 hour before

intercourse) or daily 20 mg paroxetine for the next one month. Patients were reviewed with IELT recorded in the 4th week and the side effects reviewed.

RESULTS

The mean age of participants was 34.4 years, ranging from 18 to 55 years. The mean age in dapoxetine group was 36.03 years and in paroxetine group was 32.8 years. The mean pre-treatment IELT was 39.8 seconds over all the 60 patients. Out of this, 30 patients who received dapoxetine as on demand dosing had an average IELT of 38 seconds while those receiving daily paroxetine was 41.7 seconds. In the first group receiving on demand dapoxetine, the mean IELT after 1 month of treatment was 95.06 seconds. It was an increase of 57.06 seconds over the mean pre-treatment IELT of 38 seconds. In the second group receiving daily dose of paroxetine, the mean IELT after 1 month of treatment was 106.2 seconds. It was an increase of 64.5 seconds over the mean pre-treatment IELT of 41.7 seconds. Paired t-test was used for analysis and the increase was found to be statistically significant ($p<0.05$) in both groups. An intergroup analysis was done with both equal and unequal variance, revealing statistically significant difference between the mean increase in IELT between two groups ($p = 0.01$)

Table-1: Mean IELT before and after treatment

	IELT before treatment (in seconds)	IELT at end of 1 month (in seconds)	increase in IELT (in seconds)
On demand Dapoxetine	38	95.06	57.06
Daily dosing paroxetine	41.7	106.2	64.5

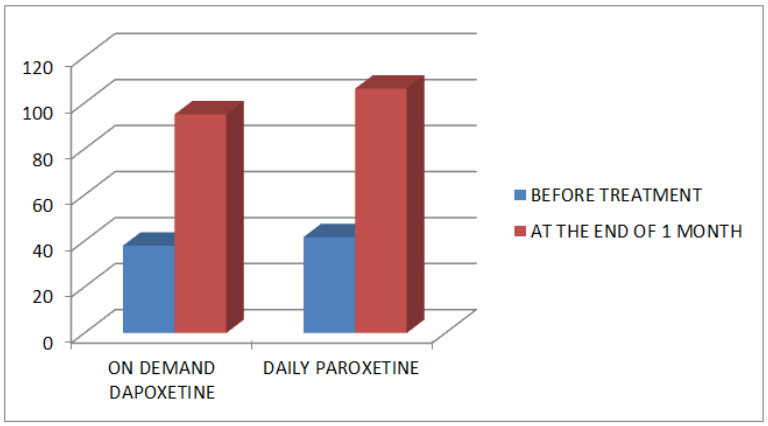

Fig-1: Mean IELT before and after 1 month

Side effects

Most of the side effects in both groups were mild and only one patient in paroxetine group discontinued the drug due to nausea. In dapoxetine group, nausea (23.3%) and headache (20%) were the most common side effects. diarrhea and dizziness was the next most common (10% each). However, all the side effects were mild and patients were able to continue the drug. Only one patient complained of a single episode of anejaculation, while none complained of decreased libido after the drug.

In the paroxetine group, nausea was the most common side effect (30%) and one patient discontinued the drug due to it. Two patients complained of more than one episodes of anejaculation. Two patients complained of decreased libido and drowsiness each. Two patients complained of insomnia and were later advised to take the drug in morning. Three patients complained of diarrhea.

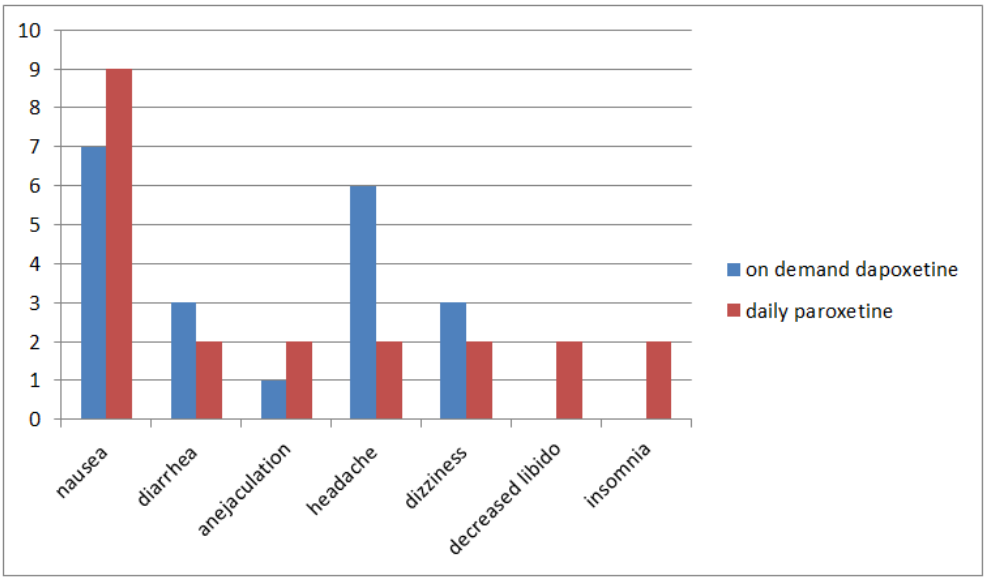

Fig-2: Side effect profile in both groups

DISCUSSION

While SSRIs have made their way in the pharmacological management of premature ejaculation, there is still no one drug, nor one dosing, which has come out to be the gold standard.

CG McMahon and K Touma [11] studied on demand paroxetine with daily dosing paroxetine and found a statistically significant superiority of daily dosing. They recommended initial daily dosing followed by an on demand dosing regimen. Dapoxetine has been studied in a dosage of 20mg, 40mg, 60mg and 100mg and has been shown to have a dose dependent increase in IELT [7,8].

In our study, both on demand 30mg dapoxetine and daily 20mg paroxetine has shown significant increase of IELT over baseline pre-treatment values. Daily dosing paroxetine has shown statistically significant more increase in IELT than dapoxetine. Side effect profile was similar in both groups with daily dosing group experiencing slightly more side effects. Nausea headache and diarrhea were the most common side effects. Anejaculation and loss of libido were rare but serious side effects.

CONCLUSION

Selective serotonin reuptake inhibitors are now the established cornerstone of the drug therapy for premature ejaculation. The choice of daily dosing or an on demand dosing should be made with the patient. Sexual habits, baseline IELT, associated erectile dysfunction, psychological stress, and the frequency of intercourse should all be taken into account. While SSRIs are both effective and tolerable, they should be a part of multimodal therapy. Proper psychological counseling and alternative therapies should be incorporated in the treatment planning for the patient. The ultimate goal is a better quality of life for the patient and his partner.

REFERENCES

1. Laumann EO, Nicolosi A, Glasser DB. Sexual problems among women and men aged 40-80 y: prevalence and correlates identified in the Global Study of Sexual Attitudes and Behaviors. Int J Impot Res. 2005 ;17(1):39-57
2. Porst H, Montorsi F, Rosen RC. The Premature Ejaculation Prevalence and Attitudes (PEPA) survey: prevalence, comorbidities, and professional help-seeking, Eur Urol. 2007;51(3):816-823.
3. Althof SE, McMahon CG, Waldinger MD. An update of the International Society of Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation (PE), J Sex Med. 2014;11(6):1392-1422.
4. Waldinger MD, Berendsen HH, Blok BF, Olivier B, Holstege G. Premature ejaculation and serotonergic antidepressants-induced delayed ejaculation: the involvement of the serotonergic system. Behavioural brain research. 1998 May 1;92(2):111-8.
5. Waldinger MD, Quinn P, Dilleen M, Mundayat R, Boolell M, Schweitzer DH. A multi-national population survey of intravaginal ejaculation latency time. In journal of sex research. 2006; 43(1): 29-29.
6. Dresser M, Lindert K, Lin D, Gidwani S, Gupta SK, Modi NB. Pharmacokinetics of single and multiple escalating doses of dapoxetine in healthy volunteers. Clinical Pharmacology & Therapeutics. 2004 Feb 1;75(2):P32-.
7. Hellstrom WJ, Althof S, Gittelman M. Dapoxetine for the treatment of men with premature ejaculation (PE): dose-fi nding analysis,J Urol,2005; 173-238.

8. Hellstrom WJ, Gittelman M, Althof S, Ho KF, Kell S. Dapoxetine HCl for the treatment of premature ejaculation: A Phase II, randomised, double-blind, placebo controlled study. J Sex Med. 2004 Nov 1;1(Suppl 1):59.
9. Pryor JL, Althof SE, Steidle C, Rosen RC, Hellstrom WJ, Shabsigh R, Miloslavsky M, Kell S, Dapoxetine Study Group. Efficacy and tolerability of dapoxetine in treatment of premature ejaculation: an integrated analysis of two double-blind randomised controlled trials. The lancet. 2006 Sep 9;368(9539):929-37.
10. Kowey PR, Mudumbi RV, Aquilina JW, DiBattiste PM. Cardiovascular safety profile of dapoxetine during the premarketing evaluation. Drugs in R & D. 2011 Mar 1;11(1):1-1.
11. Mc Mahon CG, Touma K. Treatment of premature ejaculation with paroxetine hydrochloride as needed: 2 single-blind placebo controlled crossover studies. The Journal of urology. 1999 Jun;161(6):1826-30.