Original Article

COMPARISON OF INCREASE IN INTRA-VAGINAL EJACULATORY LATENCY TIME (IELT) WITH FLUOXETINE AND PLACEBO IN PATIENTS OF PREMATURE EJACULATION

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ABSTRACT:

OBJECTIVES: Compare the mean increase in Intra-vaginal ejaculation latency time (IELT) with the fluoxetine and placebo in patients of premature ejaculation.
STUDY DESIGN: Randomized Control Trial
PLACE AND DURATION OF STUDY: Study was conducted at Department of urology, Teaching Hospital Dera Ghazi Khan, from 5th Jan 2017 to 4th Jan 2018 for period of one year.
METHODOLOGY: Eighty patients were included to compare the mean increase in intravaginal ejaculatory latency time (IELT) with fluoxetine and placebo in patients of premature ejaculation. The data was collected by a specially designed performa and the analyzed through SPSS-13.
RESULTS: Majority of the patients in both groups were found between 41-51 years of age, in Group-A 35%(n=14) and 30%(n=13) in Group-B. Mean and standard deviation was recorded as 37.49±6.536 in Group-A and 35.69± 5.493 in Group-B. The pre-intervention intravaginal ejaculatory latency time (in seconds) was recorded in Group-A 48.17±2.66 while 48.75±2.78 in Group-B, which was found insignificant, while on post-intervention was found 176.20±6.61 in Group A while 65.22±2.64 in Group-B, p-value was 0.00, and we further recorded mean increase in intravaginal ejaculatory latency time (in seconds) also which shows mean 128.02±6.51 in Group-A and only 16.47±3.86 in Group-B and it was found highly significant, p value was found 0.00 which is <0.05.
CONCLUSION: Fluoxetine is an effective drug for the treatment of premature ejaculation.
KEYWORDS: Comparison, fluoxetine, placebo, IELT, Premature ejaculation.

INTRODUCTION:

Premature Ejaculation is the discharge with slightest incitement which occurs previously or not long after vaginal entrance, that implies sooner than the patients expectation bringing about mental stress and annoyance[1].
PE is a medical condition relevant to male sexual dysfunction that stayed under estimated, undiagnosed and inappropriately treated due to patients or physicians apprehension regarding its etiology and lack of authentic treatments. PE consistently affects the men of all ages but mostly geriatrics got erectile dysfunction.[2-3]
PE is correlated with a short ejaculatory time, lack of control over ejaculation, sexual dissatisfaction for man and his accomplice, imposing adverse impact on a man's self-reliance, reduced sexual capacity and perhaps compromised quality of life in the form of interpersonal displeasure.[4]
PE is either a lifelong (present since the beginning of sexual development) or an acquired condition that develops later on after a certain period of solid sexual performance.[5] While others labeled the normal and common sexual variant as a PE because of occurrence in certain circumstances especially in men with typical ejaculatory inactivity time, yet they are

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malcontented with their timing.[6]

Penile hypersensitivity and certain frustrating conditions have been observed as causative factors in PE, while no evidential or experimental based affirmation has been given to this condition yet.[7,8] Regardless of the way that untimely discharge is caused by vascular disorder in old age men.[9] but there is no perceived organic lesion related to PE, while most recent evidence[10] calls attention to the role of prostatitis in few men with PE. Despite the fact that the physiology of patient with PE stayed flawless yet short discharge interim and absence of deliberate control causes related wretchedness. The disturbance in serotonergic system with involvement of neuro-sensory element has been expected to impact the PE.[11]

The management of PE is an developmental procedure from expert opinion based customery diagnostic treatment pattern to a more experimental and evidential approach. Among the medical modalities the topical sedatives, Alpha adrenergic antagonist receptors, tricyclic antidepressants, selective serotonin reuptake inhibitors and Phosphodiesterase-5 inhibitors were also frequently used to manage PE.[12,13]

Outcome of clinical statistics using exact endpoints was the keystone of proof based medicine, however now-a-days such evidence was confined to PE. Estimation of IELT might provide the most objective and quantitative strategy for determining the severity and treatment response of PE.[12,14] In some studies, stopwatch has been operated by patient or his partner for the calculation of cut-off value while others have rated latency based on patients and partners personal experiences.

Although, different studies showed that SSRI have treated premature ejaculation realistically, independent of type, dose, and time of convention, however SSRI are used to boost the efficacy with placebo and other drugs like opioids receptor inhibitors.[15]

We planned to conduct this study to review the effectiveness of fluoxetine for the management of patients with PE, as very few studies have been done on this subject due to social, cultural and religious reasons. The results of this study will give benefit to large number of patients alleviating their misery associated with sexual dissatisfaction and at the same time the treatment will be simple, cost effective, well-tolerated, and acceptable and with very few side effects such as dyspepsia, fatigue, yawning and perspiration.

METHODOLOGY:

Eighty patients satisfying the inclusion criteria were selected in the study from Urology OPD, Teaching Hospital, Dera Ghazi Khan. In the first appointment, after detailed explanation of the problem under study to both the subject and his spouse, an informed written consent was taken and patient's demographic profile (name, age, contact no and address) was noted. Patients were randomized into two groups by using random number table. Then all the patients were instructed to have at least one inter-course per week, and evaluated the time between penetration and ejaculation. Time evaluation was made by the wife with stop-watch marking seconds. The patients were asked to return after four weeks with IELT of four inter-courses. Initial time was obtained through the arithmetic mean of four times measured.

Group-A received fluoxetine a SSRI, 20 mg/day and Group-B received placebo (multivitamin), one tablet a day after dinner. Patients and their spouses in both groups returned 8 weeks later, bringing the ejaculatory latency time for 8 sexual inter-courses.

The final latency time was calculated by taking the arithmetic mean of IELT of 8 times measured. All the information was collected in a structured performa. The data was entered and analyzed using a modified version of SPSS-23 software program. Numerical variables like age was presented in mean and standard deviation. Mean and standard deviation was calculated for both initial and final IELT by using Student T-test taking P-value not exactly or equivalent to 0.05 as significant.

RESULTS:

Total number of 80 patients were included to compare the mean increase in intravaginal ejaculatory latency time (IELT) with fluoxetine and placebo for patients of premature ejaculation. The data was collected by a specially designed Performa and then analyzed

through SPSS-23. Age of the participants was recorded and presented in **Table No.1**, where majority of the patients in both groups were found between 41-50 years of age. In Group-A 35%(n=14) and 30%(n=12) in Group-B, Mean and standard deviation was recorded as 37.49±6.536 in Group-A and 35.69± 5.493 in Group-B.

Pre-intervention intravaginal ejaculatory latency time (in seconds) was analyzed in **Table No.2**. Mean and standard deviation of Group-A shows 48.17±2.66 while 48.75±2.78 in Group-B and this difference was insignificant, as P-value was found 0.916 which is >0.05.

Post-intervention intra-vaginal ejaculatory latency time (in seconds) was analyzed in **Table No.3**. Mean and standard deviation of Group A show 176.20±6.61 while 65.22±2.64 in Group-B and this difference was statistically significant, as P-value was found 0.00 which is <0.05.

We recorded mean increase in intravaginal ejaculatory latency time(in seconds) also which shows mean and standard deviation of Group-A 123.02±6.51 while only 16.47±3.86 in Group-B, as this difference was also highly significant because P-value was found 0.00 which is <0.05 shown in **Table No.4**.

DISCUSSION:

Premature ejaculation (PE otherwise called as quick discharge) is a common pervasive category of sexual dysfunction in men more youthful than forty years. Mostly clinicians who treats hasty ejaculation defines this condition

TABLE No. 01: AGE DISTRIBUTION (n=80)

Age (Years)	Group-A (n=40)		Group-B (n=40)	
	No of Patients	%Age	No of Patients	%Age
19-30	8	20	10	25
31-40	11	27.5	09	22.5
41-50	14	35	12	30
51-65	07	17.5	09	22.5
Total	**40**	**100**	**40**	**100**
Mean ± S.D	**37.49±6.536**		**35.69±5.493**	

Table No.2: Pre-intervention Intra-vaginal Ejaculatory Latency Time (in Seconds)

Group –A n=40	Group-B n=40
Pre- intervention IELT	**Pre- intervention IELT**
48.17±2.66	48.75±2.78

P-Value = >0.05(0.916)

Table No. 3: Post Intervention Intra-vaginal Ejaculatory Latency Time (in Seconds)

Group –A n=40	Group-B n=40
Post- intervention IELT	**Post- intervention IELT**
176.20±6.61	65.22±2.64

P-Value = <0.05(0.00)

Table No. 4: Mean Increase In Intra-vaginal Ejaculatory Latency Time (in Seconds) (n=80)

Group -A n=40	Group-B n=40
Mean Increase in IELT	**Mean Increase in IELT**
128.02±6.51	16.47±3.86

P-Value = <0.05(0.00)

as occurrence of discharge before the desire of either or both sexual partners. This broad definition thus avoids specifying a precise duration for sexual relations and reaching climax, which is erratic and dependent on different factors specific to the individuals engaging in close relations and socio-economical stress. An occasional example of premature ejaculation might be the reason of concern, yet in the event that the issue happens with half of attempted sexual relations, a dysfunctional pattern usually exists for which treatment may be admissible.

It is suggested that the treatment of premature ejaculation should endeavor to improve concerned condition as well as increased satisfaction in the patient and the partner (if he has one). Simple trials such as sexual education, awareness around sexual standards and counseling of couple are significant. It is well known fact that ladies ought to have worry about the non-penetrative sexual conduct more than men.

Selective serotonin reuptake inhibitors, which are found to concede discharge have been utilized off-mark for the management of PE for the last 10 to 20 years. The most ideal dosage and administration of SSRI for treatment of PE have not been set up, however, data showed greater success with chronic versus on-demand (PRN) dosing. Long term use of SSRIs is associated with multiple adverse effects, including dryness of mouth, nervousness, gastrointestinal upset, diarrhea, headache, drowsiness and restlessness. These AEs make current SSRIs not as much as perfect for the treatment of PE.

Emadouddin Moudi and Ali Akbar Kasaeeyan[1] elaborated in their study, the best treatment strategy of premature ejaculation is the combination of medicated and non medicated treatment. In spite of the fact that there are numerous behavioral therapies, such as squeezing and start-stop techniques but these are not properly implementable. So, the Pharmacological therapies including SSRI therapy(Citalopram, sertraline, fluoxetine, dapoxetine or paroxetine) and other oral and topical desensitizing agents are preferred due to patient convenience over the non medicated manures. As this study emphasize medical treatment as a first choice particularly SSRI that is comparable with our study.

The pleasant drug for PE should have certain qualities: (1) Its utilization ought to be reasonable, ideally oral. (2) It would have a quick beginning of activities (<60minutes).(3) It should be eliminated briskly with insignificant accumulation. (4) It should have least adverse effects with good compliance. (5) It ought to be successful on demand, irrespective of loading dose or drug dependence. (6) It should have established adequacy on IELT and patient-related result in large-scale, long term, placebo-controlled trails. None of the current off-label medication meets all these criterias.[16]

In our country very few studies have been done on this subject due to social, cultural and religious constrains. We conducted this study with the view to determine the effectiveness of fluoxetine for the management of premature ejaculation so that the results may be used for the effective management of this problem.

Post-intervention IELT (in seconds) in this study shows mean and standard deviation of Group-A 176.20±6.61 while 65.22±2.64 in Group-B which was statistically important , as P-value was found 0.00 which is <0.05 and mean increase in intra vaginal ejaculatory latency time (in seconds) in Group-A also shows highly significant, as P-value was found 0.00 which is <0.05.

The study conducted by Selahittin Çayan and Ege

Can Şerefoğlu[17] showed oral therapy of flouxetine 20-40mg per day raised IELT 5 folds that has a quite resemblance with our study where there is prolongation of IELT of about 4 fold with 20 mg dosage of fluoxetine.

A randomized clinical study conducted by Hamidreza Gholamrezaei, Ehsan Shahverdi, Saeideh Ebrahim, and keramat Dehghani[15] also authenticate present study as they assessed efficacy of fluoxetine and tramadol with regards to delaying of ejaculation. Thirty six males with premature ejaculation having mean age of 44±19.3 years were randomly assigned to receive either 50mg tramadol or 20mg fluoxetine 3 to 6 hours before sexual intercourse. Eighteen subjects were treated with fluoxetine while rest of the eighteen were treated with tramadol. Though efficacy of treatment in the two groups showed no significant difference (P value>0.05) . There was a significant difference between two groups in IELT (P value >0.05). But before - after comparison showed a significant efficacy in both groups. These findings suggest that fluoxetine is effective and safe to treat male premature ejaculation problem.

Another study conducted by M. Abu El-Hamd, A. Abdel Hamed[18]. demonstrated that the level of satisfaction score in paroxetine, dapoxetine, sildenafil and combined dapoxetine with sildenafil were fundamentally higher after treatment (P-Value =.001). After treatment with combined sildenafil and dapoxetine, the level of satisfaction score was higher as compared to the group taking single medication (P – value <.001). This study also showed that mean PEDT in paroxetine, dapoxetine, sildenafil and combined dapoxetine with sildenafil group were significantly higher after treatment (P value >.001). The means of PEDT were insignificant after treatment (P value >.05). The comparison of PEDT after treatment in different groups showed that combined dapoxetine with sildenafil is higher than other groups (P value <.001). All the treatments were well tolerated by the patients but in the combination therapy the adverse effects were also doubled. In this reference it is better to use SSRI as it is well tolerated with less side effects.

These results proposed that the better efficacy of fluoxetine in treatment of premature ejaculation is most likely due to its effect of increasing the penile sensory threshold, without changing the amplitudes and latencies of sacral evoked response and cortical somatosensory evoked potential.

Castiglione Fet al[19] study also coincides with ours as they had mentioned that the dapoxetine significantly improves IELT in patients with PE with acceptable efficacy, but still these drugs SSRIs, TAs, tramadol and PDE5 needs further research to prove their safety and effectively for the treatment of premature ejaculation that is one of the complex medical and social problem for both spouses.

Shechter A, Lowenstein L, Serefoglu EC, Reisman Y [20] described that Dapoxetine which is quickly acting SSRI with short half life, is the first endorsed oral drug for the treatment of premature ejaculation in several countries. With this medicine integrated ejaculatory latency time increases 2.5 to 3.0 fold but it differ as it is related with a lot of adverse effects and high cessation rate.

Q.Wu et al [21] study coincide with our as with sildenafil IELT was prolonged with higher frequency of weekly coitus result in the occurrence of adverse effects, though those are acceptable by the patient. It was postulated that medical therapy is superior and efficacious as compared to the psychotherapy.

The study conducted by Mohammad Che Man, Faridah Mohd Zain, Najib Majdi Yaacob, Shahidah Che Alhadi and Shaif ul Bahri Ismail[22] does not support our study as they selected 44 participants aged between 18-64 year with PEDT score of $\geq$ 9 and randomly divided participants into two groups, fluoxetine Group and dapoxetine Group. They have prescribed oral daily fluoxetine 20 mg or dapoxetine 30 mg twice weekly for 8 weeks. PE symptoms were measured by using the PE diagnostic tool and marital satisfaction score were measured using dyadic satisfaction- dyadic adjustment scale. Measurements were made at baseline and 8 weeks post intervention. At 8th week PE symptoms among participants on dapoxetine were significantly lower compared to participants on fluoxetine.

The limitation of the current study is that we did not compare Flouxetine with any other drug but the main objective was fulfilled as in our study group, the subjects achieved IELT >1 minute and got satisfaction with their sexual activity.

Another limitation was that we did not include any side effects of this drug in our study , but in our follow up experience , no complain due to this drug was recorded which further proves that this drug is safe along with the efficacy.
While the significance of this study is that very few studies have been done on this subject due to social, cultural and religious reasons, on the basis of the results of the current study, a significant benefit to a large number of patients may be given, alleviating the misery associated with sexual dissatisfaction at the treatment is also very simple, cost effective and well tolerated.

CONCLUSION:

Flouxetine in the treatment of premature ejaculation is found to be safe and compliant medicine.

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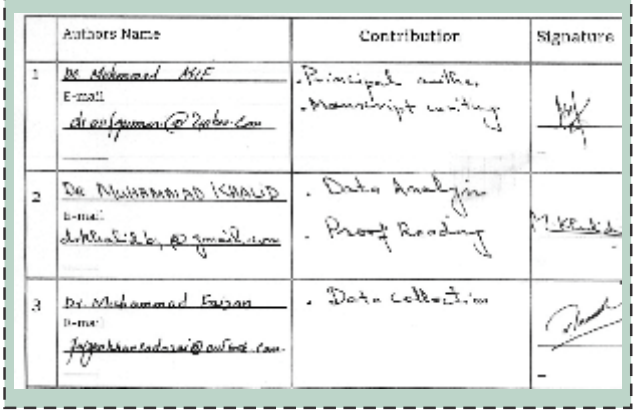

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When Imam Ali was asked about Faith in Religion, he replied that the structure of faith is supported by four pillars endurance, conviction, justice and jihad.

Hazrat Ali (Karmulha Wajhay)