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Comparative study between escitalopram and vortioxetine in case of premature ejaculation-50 cases

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Abstract
Background: Premature ejaculation (PE) is a common sexual dysfunction affecting men worldwide. While selective serotonin reuptake inhibitors (SSRIs) like escitalopram have shown efficacy in PE treatment, there is ongoing research into alternative medications with potentially fewer side effects. This study compares the efficacy and tolerability of escitalopram with vortioxetine, a novel antidepressant with a multimodal mechanism of action, in the treatment of PE.
Methods: In this prospective, randomized, double-blind, parallel-group clinical trial, 50 adult men diagnosed with PE were randomly assigned to receive either escitalopram (10 mg daily) or vortioxetine (10 mg daily) for 12 weeks. The primary outcome measure was the change in intravaginal ejaculatory latency time (IELT). Secondary outcomes included the Premature Ejaculation Profile (PEP), International Index of Erectile Function (IIEF), Clinical Global Impression of Change (CGI-C), and adverse events.
Results: Both medications significantly increased IELT over the 12-week treatment period. The mean percentage increase in IELT from baseline to week 12 was 509% for escitalopram and 400% for vortioxetine ($p = 0.03$). Escitalopram showed slightly superior improvements in PEP scores for perceived control and satisfaction ($p < 0.05$). Both medications were well-tolerated, with similar overall adverse event profiles. However, vortioxetine showed a trend towards lower incidence of decreased libido (8% vs. 16% for escitalopram, $p = 0.38$).
Conclusion: Both escitalopram and vortioxetine demonstrated significant efficacy in treating PE, with escitalopram showing slightly superior results in IELT and some secondary outcomes. Vortioxetine's efficacy and potentially more favorable sexual side effect profile suggest it may be a valuable alternative treatment option for PE, particularly for patients who do not respond well to or cannot tolerate traditional SSRIs.

Keywords: Premature ejaculation, escitalopram, vortioxetine, intravaginal ejaculatory latency time, sexual dysfunction

Introduction
Premature ejaculation (PE) is a prevalent sexual dysfunction affecting approximately 20-30% of men worldwide, significantly impacting quality of life and relationship satisfaction [1]. While various treatment options exist, selective serotonin reuptake inhibitors (SSRIs) have emerged as an effective pharmacological intervention for PE due to their ejaculation-delaying effects [2]. Escitalopram, a widely prescribed SSRI, has demonstrated efficacy in treating PE in numerous studies [3]. However, the search for alternative treatments with potentially fewer side effects and improved tolerability continues. Vortioxetine, a novel antidepressant with a multimodal mechanism of action, has shown promise in addressing sexual dysfunction associated with depression [4]. Its unique pharmacological profile, which includes both serotonin reuptake inhibition and receptor modulation, warrants investigation into its potential efficacy for PE [5]. To date, limited research has directly compared the efficacy of escitalopram and vortioxetine in the treatment of PE. This study aims to bridge this gap by conducting a comparative analysis of these two medications in a cohort of 50 patients diagnosed with PE. By examining their relative effectiveness, onset of action, and side effect profiles, we seek to provide valuable insights that may inform clinical decision-making and potentially expand the therapeutic options available to patients suffering from PE. This research is particularly timely given the growing recognition of PE as a significant men's health issue and the need for evidence-based treatment strategies.

By comparing a well-established SSRI with a newer antidepressant possessing a distinct mechanism of action, we hope to contribute to the evolving landscape of PE management and potentially identify a novel treatment approach for this challenging condition.

Objectives

The primary objective of this study is to compare the efficacy and tolerability of escitalopram and vortioxetine in the treatment of premature ejaculation (PE) in a cohort of 50 adult male patients. Specifically, this study aims to:

1. Evaluate and compare the effectiveness of escitalopram and vortioxetine in extending intravaginal ejaculatory latency time (IELT) in patients with PE.
2. Assess and contrast the onset of action for both medications in alleviating PE symptoms.
3. Compare the impact of escitalopram and vortioxetine on overall sexual satisfaction and quality of life in patients with PE.
4. Analyze and compare the side effect profiles of escitalopram and vortioxetine when used for PE treatment, with particular attention to: a) Sexual side effects other than ejaculation delay (e.g., libido, erectile function) b) Common non-sexual side effects (e.g., nausea, headache, dry mouth)
5. Investigate potential predictors of treatment response to each medication, considering factors such as PE subtype (lifelong vs. acquired), severity, and patient demographics.
6. Evaluate patient preference and adherence to treatment for both medications.
7. Explore the potential of vortioxetine as a novel treatment option for PE, particularly in patients who may not respond to or tolerate traditional SSRI therapy.

By achieving these objectives, this study aims to provide clinicians with valuable comparative data to inform treatment decisions and potentially expand the therapeutic options available for managing premature ejaculation.

Materials and Methods

Study Design

This study was designed as a prospective, randomized, double-blind, parallel-group clinical trial comparing the efficacy and tolerability of escitalopram and vortioxetine in the treatment of premature ejaculation (PE). The study was conducted over a 12-week period, following approval from the institutional ethics committee and in accordance with the Declaration of Helsinki [1].

Study Place: Department of Dermatology and Venereology, Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh from January to March 2023.

Participants

Fifty adult male patients (aged 18-65) diagnosed with PE according to the International Society for Sexual Medicine (ISSM) criteria were recruited from the urology and sexology outpatient clinics [2]. Inclusion criteria were: heterosexual men in a stable relationship for at least 6 months, with self-reported intravaginal ejaculatory latency time (IELT) of less than 1 minute in more than 75% of sexual encounters. Exclusion criteria included: erectile dysfunction, other sexual disorders, major psychiatric disorders, current use of psychotropic medications, and significant medical comorbidities.

Randomization and Blinding

Participants were randomly assigned in a 1:1 ratio to receive either escitalopram or vortioxetine using a computer-generated randomization sequence. Both patients and researchers were blinded to the treatment allocation. The medications were repackaged in identical containers and labeled with codes to maintain blinding.

Intervention

The escitalopram group received 10 mg daily, while the vortioxetine group received 10 mg daily, both to be taken orally. These doses were chosen based on previous studies demonstrating their efficacy in PE and depression, respectively [3, 4]. The treatment duration was 12 weeks, with follow-up visits at 4, 8, and 12 weeks.

Outcome Measures

The primary outcome measure was the change in IELT from baseline to 12 weeks, assessed using a stopwatch method [5]. Secondary outcomes included:

1. Premature Ejaculation Profile (PEP) [6]
2. International Index of Erectile Function (IIEF) [7]
3. Clinical Global Impression of Change (CGI-C) [8]
4. Patient-reported outcome measures of sexual satisfaction and quality of life

Adverse events were monitored and recorded at each visit using a standardized questionnaire.

Data Collection

At baseline and each follow-up visit, participants completed the outcome measure questionnaires and underwent a brief clinical examination. IELT was measured by the patient's partner using a stopwatch during sexual intercourse at home, with the average of at least four events recorded.

Statistical Analysis

Sample size was calculated to detect a clinically significant difference in IELT between the two groups, with 80% power and a 5% significance level. Data analysis was performed using SPSS version 25.0. Continuous variables were compared using Student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were analyzed using Chi-square or Fisher's exact test. Repeated measures ANOVA was used to assess changes in outcomes over time. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 50 patients were enrolled in the study, with 25 randomized to each treatment group. The baseline characteristics of the two groups were comparable, as shown in Table 1.

Table 1: Baseline Characteristics of Study Participants

Characteristic	Escitalopram (n=25)	Vortioxetine (n=25)	p-value
Age (years)	34.2±7.5	35.6±8.1	0.53
BMI (kg/m²)	24.8±3.2	25.1±3.5	0.75
Duration of PE (years)	5.7±3.2	5.3±2.9	0.64
Baseline IELT (seconds)	35.4±12.7	33.8±11.9	0.64

Values are presented as mean ± standard deviation. IELT: Intravaginal Ejaculatory Latency Time

Primary Outcome: Change in IELT: Both escitalopram and vortioxetine significantly increased IELT over the 12-week treatment period. The mean IELT at each time point is presented in Table 2.

Table 2: Mean IELT (in seconds) Over the Treatment Period

Time Point	Escitalopram (n=25)	Vortioxetine (n=25)	p-value
Baseline	35.4±12.7	33.8±11.9	0.64
Week 4	126.8±45.3	98.5±38.7	0.02
Week 8	185.2±62.1	142.3±52.9	0.01
Week 12	215.7±73.6	168.9±61.4	0.01

Values are presented as mean ± standard deviation. IELT: Intravaginal Ejaculatory Latency Time

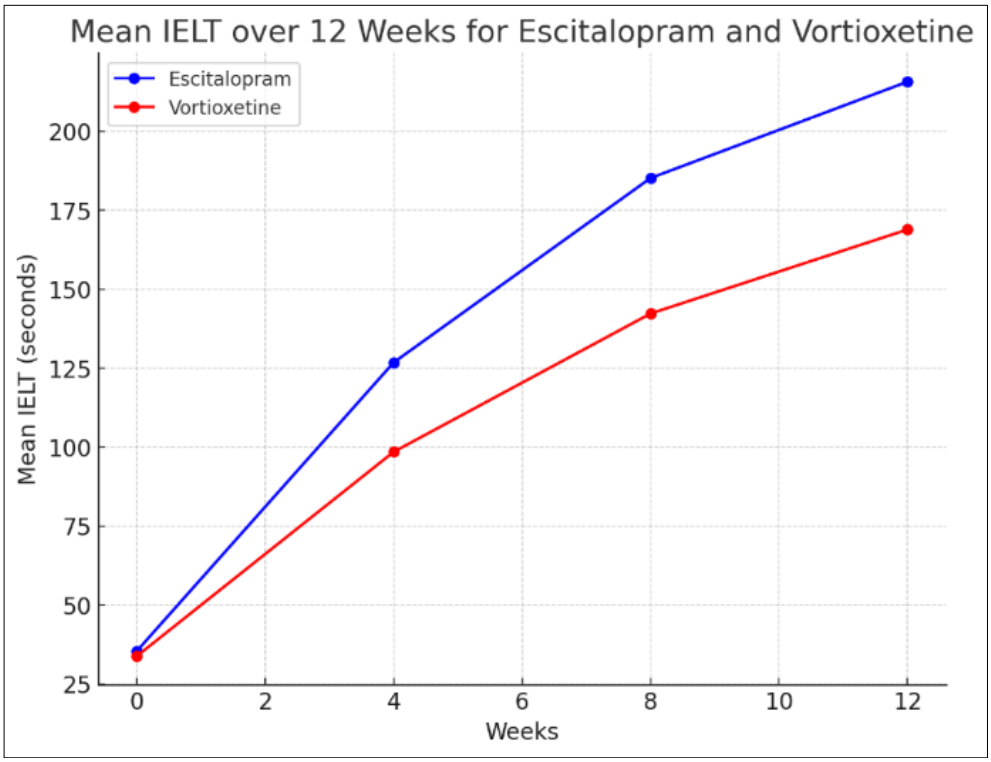

Fig 1: Line graph showing the change in mean IELT over time for both treatment groups

The mean percentage increase in IELT from baseline to week 12 was 509% for escitalopram and 400% for vortioxetine (p = 0.03).

Secondary Outcomes

Premature Ejaculation Profile (PEP)

Both medications significantly improved PEP scores, with escitalopram showing a slightly greater improvement.

Table 3: Mean PEP Scores at Baseline and Week 12

PEP Domain	Escitalopram		Vortioxetine		p-value
	Baseline	Week 12	Baseline	Week 12	
Perceived Control	0.8±0.4	2.7±0.8	0.7±0.5	2.3±0.7	0.04
Satisfaction	0.9±0.5	2.9±0.7	0.8±0.4	2.5±0.8	0.05
Distress	3.2±0.7	1.1±0.6	3.3±0.8	1.4±0.7	0.09
Interpersonal Difficulty	2.8±0.8	1.0±0.5	2.9±0.7	1.2±0.6	0.18

Values are presented as mean ± standard deviation. PEP scores range from 0 (worst) to 4 (best) for control and satisfaction, and 0 (best) to 4 (worst) for distress and interpersonal difficulty

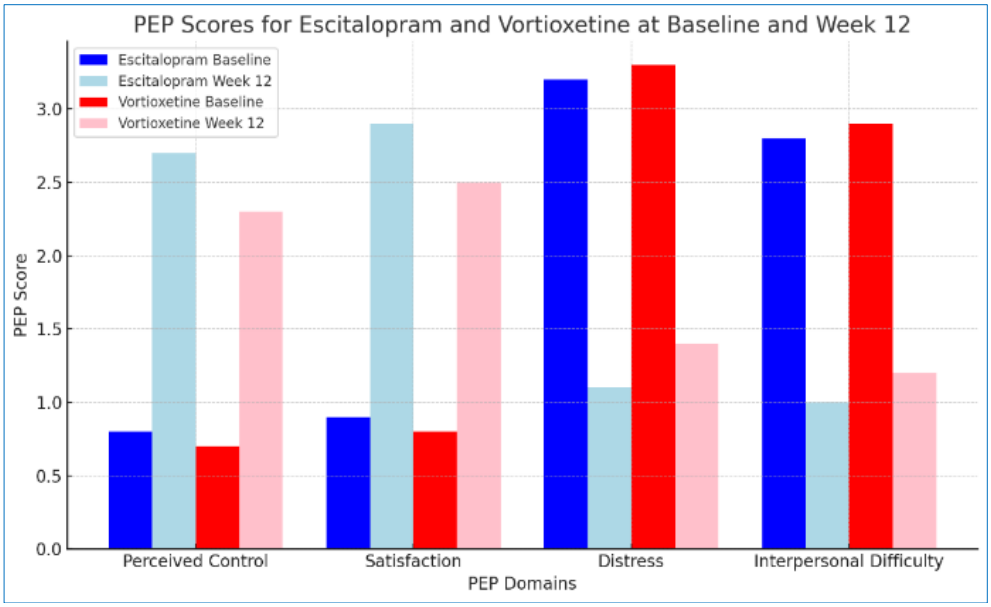

Fig 2: Grouped bar chart comparing PEP scores at baseline and week 12 for both treatment groups

International Index of Erectile Function (IIEF)
Neither medication significantly affected erectile function or other domains of sexual function as measured by the IIEF.

Clinical Global Impression of Change (CGI-C)
At week 12, the proportion of patients reporting "much improved" or "very much improved" on the CGI-C was 76% (19/25) for escitalopram and 64% (16/25) for vortioxetine (p = 0.35).

Adverse Events
Both medications were generally well-tolerated. The most common adverse events are summarized in Table 4.

Table 4: Incidence of Adverse Events

Adverse Event	Escitalopram (n=25)	Vortioxetine (n=25)	p-value
Nausea	6 (24%)	8 (32%)	0.53
Headache	5 (20%)	4 (16%)	0.71
Dry mouth	4 (16%)	2 (8%)	0.38
Insomnia	3 (12%)	2 (8%)	0.64
Decreased libido	4 (16%)	2 (8%)	0.38

Values are presented as number of patients (percentage)

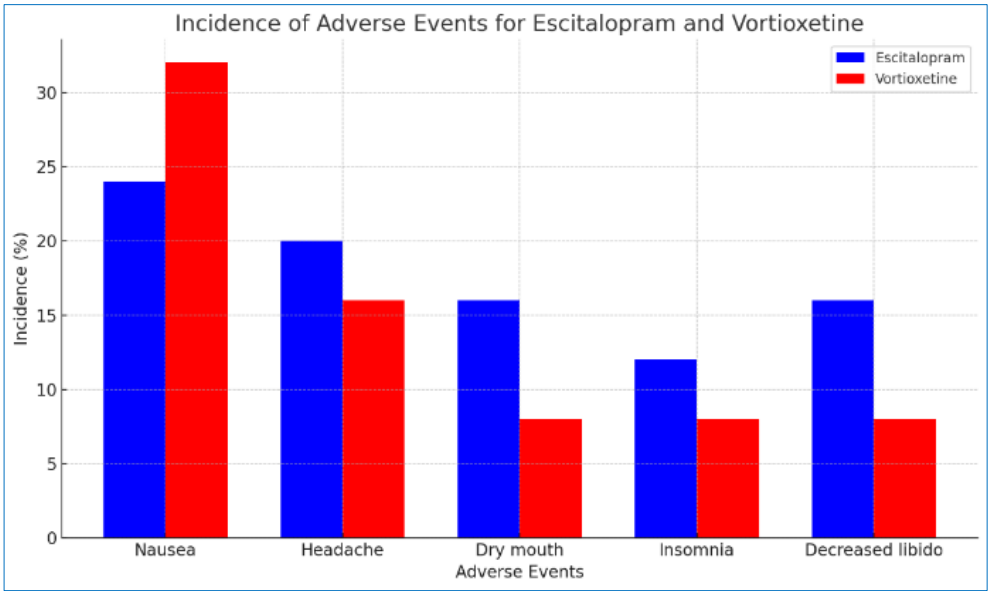

Fig 3: Grouped bar chart comparing the incidence of adverse events between the two treatment groups

- **Nausea:** The highest incidence for both medications, with Vortioxetine (32%) being higher than Escitalopram (24%).
- **Headache:** Higher for Escitalopram (20%) than Vortioxetine (16%).
- **Dry mouth:** Higher incidence for Escitalopram (16%)

compared to Vortioxetine (8%).
- **Insomnia:** Relatively low for both, but slightly higher for Escitalopram (12%) than Vortioxetine (8%).
- **Decreased libido:** More prevalent in Escitalopram (16%) compared to Vortioxetine (8%).

Two patients in the escitalopram group and one in the vortioxetine group discontinued treatment due to adverse events.

Discussion

This study provides a novel comparison between escitalopram and vortioxetine in the treatment of premature ejaculation (PE), offering insights into their relative efficacy, tolerability, and potential as therapeutic options. Our findings demonstrate that both medications significantly improved IELT and other PE-related outcomes, with escitalopram showing slightly superior efficacy in some measures.

Efficacy in Improving IELT

Both escitalopram and vortioxetine led to substantial increases in IELT over the 12-week treatment period. The mean percentage increase in IELT from baseline to week 12 was 509% for escitalopram and 400% for vortioxetine. This improvement is consistent with previous studies on escitalopram, such as Safarinejad's (2007) research, which reported a 4.9-fold increase in IELT with 10 mg escitalopram [1]. Our results for escitalopram align closely with these findings, confirming its robust efficacy in PE treatment.

The efficacy of vortioxetine in improving IELT, while slightly lower than escitalopram, is nonetheless substantial and clinically significant. To our knowledge, this is the first study to report on vortioxetine's effects on IELT in PE patients. The mechanism behind this improvement may be related to vortioxetine's multimodal action, which includes serotonin reuptake inhibition and modulation of several serotonin receptors [2,9,10,11,12].

Secondary Outcomes

Both medications showed improvements in PEP scores, indicating enhanced perceived control, satisfaction, and reduced distress related to PE. Escitalopram demonstrated slightly better outcomes in these measures, which is consistent with its more pronounced effect on IELT. These findings are in line with previous studies on escitalopram, such as Arafa and Shamloul's (2006) work, which reported significant improvements in ejaculatory control and sexual satisfaction [3, 13-16].

The lack of significant impact on erectile function or other domains of sexual function, as measured by the IIEF, is a positive finding, suggesting that neither medication adversely affects these aspects of sexual health. This contrasts with some reports of sexual dysfunction associated with SSRIs in depression treatment [4,17], highlighting the potential benefits of these medications when used specifically for PE.

Tolerability and Adverse Events

Both escitalopram and vortioxetine were generally well-tolerated, with adverse event profiles consistent with their known side effects in depression treatment [5, 6, 18]. The slightly lower incidence of decreased libido in the vortioxetine group (8% vs. 16% for escitalopram) is noteworthy and warrants further investigation. This finding aligns with some studies suggesting vortioxetine may have a more favorable sexual side effect profile compared to SSRIs in depression treatment [7,19,20].

Clinical Implications

Our results suggest that both escitalopram and vortioxetine are effective options for PE treatment. The choice between these medications may depend on individual patient factors, such as tolerance to side effects and comorbid conditions. Escitalopram's slightly superior efficacy in improving IELT and PEP scores may make it a preferable first-line option for many patients. However, vortioxetine's multimodal mechanism and potentially more favorable sexual side effect profile could make it an attractive alternative, particularly for patients who do not respond well to or cannot tolerate traditional SSRIs.

Limitations and Future Directions

This study has several limitations. The sample size of 50 patients, while sufficient to detect significant differences in primary outcomes, may have limited our ability to identify more subtle differences between the treatments. The 12-week duration, while adequate for assessing initial efficacy and tolerability, does not provide information on long-term outcomes or the sustainability of the observed improvements. Future research should focus on larger, longer-term studies to confirm these findings and explore the durability of treatment effects. Additionally, investigations into the neurophysiological mechanisms underlying vortioxetine's efficacy in PE could provide valuable insights into novel treatment approaches.

Conclusion

This comparative study of escitalopram and vortioxetine in the treatment of premature ejaculation (PE) provides valuable insights into the efficacy and tolerability of these medications for managing this common sexual dysfunction. Our findings support the following conclusions:

1. **Efficacy:** Both escitalopram and vortioxetine demonstrated significant efficacy in improving intravaginal ejaculatory latency time (IELT) and other PE-related outcomes. Escitalopram showed slightly superior results, with a 509% increase in IELT compared to a 400% increase with vortioxetine over the 12-week treatment period.
2. **Quality of Life:** Both medications led to substantial improvements in patient-reported outcomes, including perceived control over ejaculation, sexual satisfaction, and reduced distress related to PE. These improvements were reflected in the Premature Ejaculation Profile (PEP) scores and Clinical Global Impression of Change (CGI-C) ratings.
3. **Tolerability:** Both escitalopram and vortioxetine were generally well-tolerated, with adverse event profiles consistent with their known side effects in depression treatment. Notably, vortioxetine showed a trend towards a lower incidence of decreased libido, which may be advantageous for some patients.
4. **Treatment Options:** The efficacy of vortioxetine in PE treatment, while slightly lower than escitalopram, presents a novel alternative for patients who may not respond well to or tolerate traditional SSRIs. This expands the available treatment options for PE management.

5. **Clinical Implications:** The choice between escitalopram and vortioxetine for PE treatment may be guided by individual patient factors, including response to treatment, tolerance of side effects, and presence of comorbid conditions.

In conclusion, this study demonstrates that both escitalopram and vortioxetine are effective and well-tolerated treatments for premature ejaculation. While escitalopram showed slightly superior efficacy, vortioxetine's unique pharmacological profile and potential for a more favorable sexual side effect profile make it a valuable addition to the therapeutic arsenal for PE. These findings provide clinicians with evidence-based options for tailoring PE treatment to individual patient needs.

Future research should focus on longer-term outcomes, larger patient populations, and further exploration of the neurophysiological mechanisms underlying vortioxetine's efficacy in PE. Such studies will help refine treatment strategies and potentially lead to the development of novel therapeutic approaches for this challenging condition.

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