

# Comparing the Effectiveness of Tramadol versus Paroxetine in the Treatment of Premature Ejaculation

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## Author's Contribution

<sup>1,4</sup>Substantial contributions to the conception or design of the work or the acquisition, methodology, analysis,<sup>3</sup> Final approval of the version to be published.<sup>2,5</sup>Active Participation in active,<sup>6</sup>Drafting the work or revising it critically for important intellectual content

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## ABSTRACT

**Objective:** To conduct a comparative analysis of the effectiveness of tramadol versus paroxetine in managing premature ejaculation (PE).

**Methodology:** This study employs a randomized, double-blind, parallel-group design conducted at the Urology department of Liaquat University of Medical and Health Sciences Jamshoro, Hyderabad, Pakistan. Participants are adult males aged 18–65 years who report persistent PE were included in the study. Premature ejaculation occurs in men when semen leave the body (ejaculate) sooner or just before penetration. Participants meeting the diagnostic criteria for PE are assigned randomly to either the tramadol group or the paroxetine group. Participants in the tramadol group receive oral tramadol hydrochloride at a dose of 50 mg, taken 1–2 hours before anticipated sexual activity. Participants in the paroxetine group receive oral paroxetine hydrochloride (20mg daily), taken continuously for 8 weeks. The primary outcome measure is the change or delay in intravaginal ejaculatory latency time (IELT).

**Results:** The mean baseline IELT and after treatment IELT in tramadol group was statistically significant ( $p < 0.001$ ),  $47.83 \pm 5.68$  seconds and  $141.54 \pm 4.04$  seconds, respectively. Similarly, the mean baseline IELT and after treatment IELT in the paroxetine group was statistically significant ( $p < 0.001$ ),  $47.03 \pm 5.48$  seconds and  $98.67 \pm 4.68$  seconds, respectively.

**Conclusion:** Tramadol is an effective alternative to paroxetine in treating premature ejaculation, with studies showing it significantly delays ejaculation similar to paroxetine, providing patients more options for managing lifelong PE.

**Keywords:** Premature ejaculation, Paroxetine, Tramadol, Efficacy, intravaginal ejaculatory latency time.

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## Introduction

Premature ejaculation (PE), a usual dysfunction of sexual intercourse that affects 20% to 40% of male worldwide, not only diminishes sexual satisfaction but also causes significant mental distress and strains interpersonal relationships.<sup>1</sup> Despite its prevalence, the definition and characterization of PE remain elusive, with no universally accepted diagnostic criteria.<sup>2</sup> As per guidelines of

International Society of Sexual Medicine (ISSM), PE is defined as persistent or recurrent early ejaculation occurring within one minute prepenetration in vagina and also associated with interpersonal difficulty and distress.<sup>3</sup>

Premature ejaculation is classified into two types: primary which is lifelong and secondary that is also called acquired, with the latter being more common.<sup>4</sup> The management of PE includes both non-pharmacological and pharmacological methods. Among pharmacological

treatments, selective serotonin reuptake inhibitors (SSRIs), antidepressants, opioid agonists, alpha-1 adrenoreceptor antagonists, phosphodiesterase type 5 inhibitors, and local anesthetics are used.<sup>5</sup> However, no pharmacological treatments are officially recommended for PE. Paroxetine, an SSRI, is effective in delaying ejaculation and can be administered either on-demand or daily, although SSRIs may not always be effective. Tramadol, an opioid receptor agonist, is also effective in treating PE.<sup>6</sup>

Tramadol is a centrally acting opioid analgesic that has been found to have potential benefits in the treatment of PE.<sup>7</sup> Tramadol works by hindering the norepinephrine and serotonin reuptake, which may help in prolonging ejaculation. Numerous studies have reported the efficacy of this drug in intravaginal prolongation of ejaculation latency time and also help in sexual satisfaction and PE improvement in male partners.<sup>8</sup> But, it's also having a risk of adverse effects like dizziness, nausea, constipation and dependency.<sup>9</sup>

Another selective serotonin reuptake inhibitor is Paroxetine which is also an antidepressant and more often prescribed for PE due to its ability of delayed ejaculation.<sup>10</sup> Its mechanisms are enhanced serotonin levels in the brain that initiate the ejaculatory reflex in return. Some previous clinical trials<sup>11</sup> have reported that paroxetine has the ability to enhance IELT to a significant range and also plays an important role in PE level in males.<sup>12</sup>

Despite the existence of studies on the on-demand use of paroxetine versus tramadol for PE management, there is a noticeable lack of comprehensive local data.<sup>13,14</sup> This study aims to compare the efficacy of paroxetine versus tramadol in the treatment of PE, providing vital insights for local healthcare professionals and enhancing the quality of care for patients with PE.

## Methodology

This randomized, double-blind, parallel-group design study was conducted at the Urology department of Liaquat University of Medical and Health Sciences Jamshoro, Hyderabad, Pakistan. Participants meeting the diagnostic criteria for PE are randomly assigned to either the tramadol group or the paroxetine group. Premature ejaculation occurs in men when semen leave the body (ejaculate) sooner or just before penetration. The study adheres to ethical guidelines and obtains informed consent from all participants. Participants are adult males aged 18–65 years who report persistent PE. Exclusion criteria include

contraindications to tramadol or paroxetine, history of substance abuse, psychiatric disorders, or concurrent use of medications affecting sexual function.

Sample size is calculated based on previous studies, aiming for 80% power to detect a clinically significant difference in IELT between groups. Control over ejaculation in the tramadol group was 24.5 and in the Paroxetine group 49.1%.<sup>15</sup> A sample size of 100 participants per group is planned, considering potential attrition.

Participants in the tramadol group receive oral tramadol hydrochloride at a dose of 50 mg, taken 1–2 hours before anticipated sexual activity. Participants in the paroxetine group receive oral paroxetine hydrochloride at a dose of 20 mg daily, taken continuously for 8 weeks. Main outcome was prolongation of IELT

The primary outcome measure is the change in intravaginal ejaculatory latency time (IELT) from pretreatment to completion of course. Other outcomes include changes in self-reported ejaculatory control, sexual satisfaction, and adverse events.

Baseline assessments include demographic information, medical history, and baseline IELT measurement. Follow-up assessments occur at weeks 2, 4 and 8, comprising IELT measurement, self-reported ejaculatory control, and adverse event monitoring.

Data analysis involves SPSS interpretation. Between-group differences in IELT and secondary outcomes are analyzed using independent t-tests or non-parametric equivalents. Adverse events are compared using chi-square tests.

## Results

Among 200 patients, 100 patients were included in the tramadol group and 100 patients were included in the paroxetine group. The average (Mean±SD) age of tramadol and paroxetine group was 35.77±5.92 years and 36.35±5.55 years, respectively, (p=0.403). The mean baseline IELT and after treatment IELT in tramadol group was statistically significant (p<0.001), 47.83±5.68 seconds and 141.54±4.04 seconds, respectively. Similarly, the mean baseline IELT and after treatment IELT in the paroxetine group was statistically significant (p<0.001), 47.03±5.48 seconds and 98.67±4.68 seconds, respectively. (Table I).

**Table I: Age and IELT among the groups.**

Variable	Tramadol Group	Paroxetine Group	p-value
Mean±SD			
Age (years)	35.77±5.92	36.35±5.55	0.403
Baseline IELT (seconds)	47.83±5.68	47.03±5.48	0.312
Treatment IELT (seconds)	141.54±4.04	98.67±4.68	<0.001
p-value	<0.001	<0.001	

The mean after treatment PE was significantly increased from the baseline PE in tramadol and paroxetine groups, ( $p<0.001$ ). The satisfaction with sexual intercourse baseline and after treatment in tramadol and paroxetine group was almost the same, and not statistically significant, ( $p>0.050$ ). (Table II).

**Table II: Comparison of primary measures between groups.**

Variable	Tramadol Group	Paroxetine Group	p-value
Mean±SD			
Baseline PE	10.17±1.72	10.15±1.88	0.938
Treatment PE	15.43±2.68	8.10±0.91	<0.001
p-value	<0.001	<0.001	
Intercourse satisfaction (Baseline)			
N (%)			
Ejaculatory control	64 (64.0)	58 (58.0)	0.384
Difficulty	13 (13.0)	8 (8.0)	0.249
Ejaculation-related distress	28 (28.0)	22 (22.0)	0.327
Intercourse satisfaction (Post-treatment)			
Ejaculatory control	31 (31.0)	32 (32.0)	0.879
Difficulty	12 (12.0)	7 (7.0)	0.228
Ejaculation-related distress	23 (23.0)	13 (13.0)	0.066

## Discussion

Premature ejaculation (PE) significantly impacts sexual satisfaction for couples, necessitating effective treatments to enhance their sexual life. Due to PE's uncertain and multifaceted etiology, there is no standardized treatment protocol, resulting in diverse therapeutic approaches.<sup>16</sup> These include behavioral therapy to modify actions and delay ejaculation, sexual education to provide knowledge and management techniques, and pharmaceutical treatments to delay ejaculation or address underlying issues contributing to PE.<sup>17</sup>

Climacteric and regional variations may influence latency time, an Egyptian study<sup>18</sup> revealed that 2.5% of men had an intravaginal ejaculation latency time of less than one minute and 6% had a latency time of less than two minutes. Rapid ejaculation can be treated pharmacologically with

various medications that act either centrally or locally to delay ejaculation and subsequent orgasm.

In the present study, significant PE improvement was noted when tramadol was used in place of paroxetine. Hamidi-Madani et al<sup>19</sup> supported our findings, suggesting that paroxetine can be replaced with tramadol, as tramadol is also effective and safe in use in patients who require PE treatment. Three groups Tramadol, Placebo and paroxetine were compared in this study. The increase in the tramadol group ( $136.98\pm77.27$ ) was significantly greater than that in the paroxetine group ( $91.17\pm73.22$ ) and the placebo group ( $77.97\pm54.96$ ), with a p-value of less than 0.0001. Conversely, Zhang et al<sup>20</sup> supported paroxetine as it is found to have more effective and longer-lasting PE results as compared to tramadol. However, they noted that the efficacy of paroxetine is further enhanced when used in combination with other treatments.

Supporting these findings, research conducted by Kaynar et al<sup>21</sup> also observed a significant increase in mean IELT after eight weeks of treatment with Tramadol, compared to placebo, for patients with premature ejaculation (PE). Conversely, a study by Alghobary et al<sup>22</sup> presented controversial results: at the six-week mark, both Paroxetine and Tramadol were found to significantly increase IELT, by eleven-fold and seven-fold respectively. However, by the 12th week, Tramadol's effectiveness declined, decreasing the IELT by five-fold, whereas Paroxetine continued to be effective, increasing the IELT by twenty-two-fold.

Wu et al<sup>23</sup> conducted a study that concluded there was no significant difference in mean Intravaginal Ejaculatory Latency Time (IELT) between tramadol and paroxetine. Their findings suggest that tramadol can be considered a viable treatment option for premature ejaculation (PE). In similar research conducted by Safarinejad et al<sup>24</sup> demonstrated that tramadol is an effective drug in treatment of PE and prolongs the IELT when given at least for 6 weeks and longer, these results are consistent with our study results.

Rehman et al<sup>15</sup> reported that premature ejaculation can be treated with Tramadol successfully; its ejaculation control was reported 24.5% in this study population, its associated distress and difficulty in ejaculation was reported 7.5%. In another study Valecha et al<sup>25</sup> reported that on comparison of tramadol and paroxetine, it was observed that Tramadol was more effective in ejaculation delay and PE management. Observation of this study suggested that tramadol might be a strong alternative to paroxetine in

long term outcomes and PE management. But further research is needed.

## Conclusion

Tramadol is a safe and effective replacement drug of paroxetine in management of premature ejaculation, previous research evidence also favors its ability to delay ejaculation similar to paroxetine, providing a more suitable option to patients in managing PE.

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