Paroxetine Treatment of Premature Ejaculation: A Double-Blind, Randomized, Placebo-Controlled Study

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Seventeen male outpatients with premature ejaculation were randomly assigned to treatment with paroxetine (N=8) or placebo (N=9). After a first week dose of 20 mg/day, the paroxetine regimen was increased to 40 mg/day for 5 weeks. Patients and their female partners were interviewed separately. Patients treated with paroxetine had significantly greater clinical improvement than the patients given placebo.
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In DSM-III-R, premature ejaculation is defined as persistent or recurrent ejaculation with minimal sexual stimulation or before, upon, or shortly after penetration and before the person wishes it. In operational terms, premature ejaculation has been defined in terms of varying durations of intravaginal contact and number of thrusts before ejaculation, but a consensus regarding its operational definition has not been reached (1). This double-blind, randomized, placebo-controlled study was designed to investigate the efficacy and side effects of the new serotonergic antidepressant paroxetine on postponing ejaculation in patients with premature ejaculation.

METHOD

The subjects were 17 adult male outpatients and their female partners. Twelve patients were selected through an advertisement, and five were drawn from a waiting list for psychosexual therapy of a sexology outpatient department.

Premature ejaculation was defined as intravaginal ejaculation latency time that was less than 2 minutes after vaginal intromission and occurred in more than 50% of sexual intercourses. After telephone screening, patients and their partners were seen at the sexology department of the psychiatric outpatient department. Informed consent was obtained before inclusion in the study.

Inclusion criteria were that the subjects be heterosexual, be aged 18–75, experience premature ejaculation, and be involved in a steady sexual relationship with a female partner who was able to participate in the study. Exclusion criteria were erectile dysfunction, inhibited male orgasm, alcohol and substance abuse, mental disorders, physical illnesses, and the use of medication, including psychoactive medication.

Patients were randomly assigned to either paroxetine or placebo treatment. Capsules were identical, with each capsule of active drug containing 20 mg of paroxetine. One capsule/day had to be taken during the first week of treatment and two capsules/day from the onset of week 2 until the end of week 6. The capsules were taken after breakfast. Patients and their partners attended the outpatient department a few days before the start of treatment and at the end of weeks 3 and 6. Seven days after the start of treatment, the patient had telephone contact with the interviewer before increasing the daily dose.

During the study the patients did not use condoms or topical anesthetics. Patients and their partners allocated scores separately and were interviewed individually by the first author. All measurements were obtained before treatment and at the end of weeks 3 and 6. Psychopathology in the patients was screened according to the SCL-90 (2). Both patients and their partners were also issued a questionnaire, which we designed, that contained items such as the in-

TABLE 1. Characteristics of Men With Premature Ejaculation Treated With Paroxetine or Placebo

Characteristic	Paroxetine (N=8)		Placebo (N=9)		p[a]
	Median	*Range*	*Median*	*Range*	
Age of patients (years)	41	27–48	38	30–47	0.88
Age of partners (years)	40	24–47	36	21–45	0.47
Duration of relationship (years)	16	1–20	9	0.5–20	0.11
	N	%	*N*	%	
Onset of premature ejaculation					0.99
Primary (lifelong)	7	87.5	7	77.8	
Secondary (acquired)[b]	1	12.5	2	22.2	
Method of selection					0.99
Advertisement	6	75.0	6	66.7	
Waiting list	2	25.0	3	33.3	

[a]Difference between median values; Mann-Whitney test and Fisher's exact test.
[b]Onset was at least 2 years earlier.

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TABLE 2. Intravaginal Ejaculation Latency Time and Number of Thrusts Until Ejaculation as Assessed by Men With Premature Ejaculation Treated With Paroxetine or Placebo and by Their Partners

	Patient Assessment					Partner Assessment				
	Paroxetine (N=6)		Placebo (N=8)			Paroxetine (N=6)		Placebo (N=8)		
Measure and Time	Median	Range	Median	Range	p[a]	Median	Range	Median	Range	p[a]
Intravaginal ejaculation latency time										
Before treatment	30 sec	3–40 sec	15 sec	5–90 sec	0.70	10 sec	3–30 sec	30 sec	5–90 sec	0.21
After 3 weeks	7.5 min	3.0–20.0 min	20 sec	5–120 sec	0.002	8.5 min	2.0–17.5 min	23 sec	5–60 sec	0.002
After 6 weeks	10.0 min	5.0–20.0 min	15 sec	5–120 sec	0.002	10.0 min	5.0–17.5 min	33 sec	10–90 sec	0.003
Number of thrusts										
Before treatment	4.0	2.5–9.0	4.0	1.5–9.0	0.99	2.5	1.0–9.0	5.0	2.5–12.5	0.13
After 3 weeks	>30	all >30	5.5	1.5–12.5	0.001	>30	all >30	5.5	2.5–17.5	0.01
After 6 weeks	>30	22.0– >30	5.0	2.0–9.0	0.001	>30	22.0– >30	6.0	2.0–12.0	0.001

[a]Difference between median values; Mann-Whitney test.

travaginal ejaculation latency time, the number of thrusts before ejaculation, intercourse frequency, libido, and possible side effects. Side effects were scored on 5-point ordinal scales ranging from none to very severe.

These variables were scored, and mean or median values (standard deviation or range) were computed for the two groups of patients separately. Because of the strongly skewed distribution of the efficacy parameters, nonparametric statistical tests were used to assess differences in the measurements at the three time points within the treatment groups (Friedman two-way analysis of variance [ANOVA] and Wilcoxon matched-pairs signed-ranks test) and between the groups (Mann-Whitney test). The relation between parameters was quantified by using the Spearman rank correlation coefficient. Differences between groups on discrete variables were tested for statistical significance by using Fisher's exact test. Differences between the two treatment groups on the SCL-90 profile and their changes over time were analyzed by using multivariate repeated measures ANOVA. A two-tailed p value ≤0.05 was considered significant.

RESULTS

Seventeen patients and their female partners participated in the study. Primary (lifelong) and secondary (acquired, onset at least 2 years earlier) premature ejaculation were experienced by 14 and three patients, respectively. Of the 17 patients, eight were randomly assigned to the paroxetine group and nine to the placebo group (table 1). Because of side effects experienced, one patient from each group withdrew from the study during the first week of treatment. In week 3, one patient from the paroxetine group reported a retarded ejaculation of up to 30 minutes. Reducing his dose to one capsule/day resulted in an intravaginal ejaculation latency time of 7 minutes. The analysis of the results is confined to the remaining 14 patients who completed the entire study (table 2).

Before treatment, most patients experienced intravaginal ejaculation within 40 seconds of intromission; only one patient had an intravaginal ejaculation latency time of 90 seconds. The assessments of the partners for the intravaginal ejaculation latency time showed good agreement with those of the patients: the correlation was 0.55 before treatment and increased to 0.96 after 6 weeks.

In the paroxetine group the median intravaginal ejaculation latency time increased from 30 seconds (before treatment) to 7.5 minutes after 3 weeks and to 10.0 minutes after 6 weeks according to the patients themselves, and from 10 seconds (before treatment) to 8.5 and 10.0 minutes, respectively, according to their partners. The overall increase is statistically significant (patient assessments: Friedman $\chi^2=9.75$, df=2, p=0.008; partner assessments: Friedman $\chi^2=9.33$, df=2, p=0.009) but not the increase between weeks 3 and 6 (Wilcoxon z=–1.60, p=0.11 and Wilcoxon z=–1.28, p=0.20 for patient and partner assessments, respectively). The number of thrusts increased for all patients in the paroxetine group from four (before treatment) to over 30 in week 3, as well as in week 6 (Friedman $\chi^2=9.08$, df=2, p=0.01). Their partners counted the same numbers. In the placebo group no statistically significant differences were found. The change in the intravaginal ejaculation latency time and the number of the thrusts between the start of treatment and week 3 or week 6 was significantly different between groups whether according to the patients or according to their partners (Hotelling's F=63.4, df=8, 36, p<0.001).

No statistically significant differences were found between groups with respect to the mean weekly frequency of intercourse, although after 3 weeks there was a remarkable increase in the paroxetine group. After 3 and 6 weeks, patients in the paroxetine group reported an increase in libido (defined as sexual desire), although not a statistically significant one.

The SCL-90 provided no statistically significant differences between the two groups of patients or within the treatment groups. The mean scores on subscales of the SCL-90 were higher than those of the normal population but lower than scores for the psychiatric outpatient population.

No statistically significant differences were found with respect to side effects of treatment, either between the two groups of patients or among the three time points within the groups. However, most patients in the paroxetine treatment group complained of fatigue and bursts of frequent intense yawning. Nearly all patients reported an immediate slight improvement in ejaculatory latency during the first week of treatment.

DISCUSSION

In the present study, the use of paroxetine resulted in a remarkable extension of intravaginal ejaculation latency time in patients with premature ejaculation. The intravaginal ejaculation latency time was assessed by separate questioning of patients and partners concerning their subjective experience. Agreement was found between patients and partners. Even before treatment, when patients and partners did not have the opportunity to discuss this topic with each other, the correlation between men and women was good (0.55). The fact that the correlation was stronger after 6 weeks (0.96) can of course be attributed to the patients and partners having the chance to discuss this issue with each other before visiting the outpatient department and also to the dramatic increase in the variation of time to ejaculation.

In our opinion, the dramatic improvement in intravaginal ejaculation latency time, which began during the first days of treatment, may well be a direct effect of blocking central serotonin reuptake and cannot be ascribed to a decrease of psychopathology, since the improvement in premature ejaculation was not accompanied by a significant decrease in anxiety, depression, or other items on the SCL-90.

Treatment of premature ejaculation with low doses of clomipramine has been shown to be effective in double-blind studies (3, 4). However, its application in high doses is complicated by anticholinergic side effects, loss of libido, and genital anesthesia (3, 4). In our study, anticholinergic side effects and side effects of paroxetine on erectile function and libido were not reported.

Although the effect of paroxetine on postponement of ejaculation within a period of 6 weeks is remarkable, we have no information on long-term use of paroxetine, nor do we know whether premature ejaculation reappears after discontinuing the drug.

The intravaginal ejaculation latency time changed dramatically at a dose of 40 mg/day, but it is possible that 20 mg/day might also be sufficient. One might further speculate that the combination of paroxetine and psychosexual therapy could offer an effective treatment in the long run.

In conclusion, our findings support the view that paroxetine offers a good pharmacotherapeutic treatment for premature ejaculation in patients who have no further psychopathology because of its dramatic postponement of ejaculation, the rapidity of the improvement, its lack of influence on libido and erectile functioning, and its mild side effects.

In future studies, currently underway, we will investigate the dose-response relation of paroxetine and premature ejaculation, the effect of paroxetine on premature ejaculation in the long term, and the role of central serotonergic mechanisms in the pathogenesis of human ejaculation disorders.

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