

COMPARISON OF EFFICACY OF SILDENAFIL-ONLY, SILDENAFIL PLUS TOPICAL EMLA CREAM, AND TOPICAL EMLA-CREAM-ONLY IN TREATMENT OF PREMATURE EJACULATION

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ABSTRACT

Objectives. To compare the efficacy of sildenafil (Viagra) only, sildenafil plus topical anesthetic cream (EMLA), and topical EMLA-cream-only to that of placebo in treating premature ejaculation.

Methods. A total of 84 patients were enrolled in this study. The duration of premature ejaculation in the patients ranged from 9 to 60 months (mean 32.5 ± 14.6). Patients were randomized into four groups. Group 1 consisted of 20 patients who took placebo for 2 months. Groups 2 and 3 consisted of 20 and 22 patients, respectively, and they received 50 mg sildenafil 45 minutes before coitus for 2 months. In addition, patients in group 3 applied topical EMLA cream to the glans penis 15 minutes before coitus. The 22 patients in group 4 used topical EMLA-cream-only. After at least eight sexual attempts, the patients' clinical responses were assessed using the patient self-description method. Effectiveness was described as improvement plus cure.

Results. The effectiveness was 40% in group 1, 55% in group 2, 86.4% in group 3, and 77.3% in group 4. Of the groups, a significant difference was found in the effectiveness of the treatments (Pearson chi-square = 0.00). No significant difference was found between groups 1 and 2 ($P = 0.26$). Efficacy was more successful in groups 3 and 4 than in the others ($P = 0.00$). The difference between groups 3 and 4 was not significant (Pearson chi-square = 0.42).

Conclusions. Sildenafil-only was not superior to placebo or combination treatment. Topical EMLA-cream-only had equal effectiveness to that of sildenafil plus topical EMLA treatment. The use of topical EMLA-cream-only seems to be an effective treatment of premature ejaculation. UROLOGY 67: 388–391, 2006. © 2006 Elsevier Inc.

Premature ejaculation (PE) has been reported as the most common sexual dysfunction in men.¹ Data from the National Health and Social Life Survey have revealed a prevalence of 21% in men aged 18 to 59 years in the United States.² The exact etiology of PE is not well understood, although it is well-recognized that ejaculation latency is primarily affected by psychological, cognitive, and somatic factors.³ Behavioral therapy and psychologi-

cal counseling are the initial approaches in the treatment of PE. However, these techniques require active involvement of the patients and their partners. Some cultural and socioeconomic groups may not be comfortable participating in these therapies. Therefore, some pharmacologic agents have been recommended for those in whom the behavioral approach is unsuccessful.^{4,5}

Some selective serotonin re-uptake inhibitors have been used to treat this sexual problem, with varying degrees of success.^{6–8} Additionally, new treatment regimens have been investigated as a treatment option for PE. Currently, two new treatments, topical anesthetic agents and oral sildenafil, have been considered for PE treatment.³ Topical anesthetic agents are applied to the glans penis before intercourse to delay ejaculation.⁹ Sildenafil is a selective cyclic guanosine monophosphate-

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Submitted: April 16, 2005, accepted (with revisions): September 7, 2005

TABLE I. Patient characteristics

	Group 1 (n = 20)	Group 2 (n = 20)	Group 3 (n = 22)	Group 4 (n = 22)	P Value
Age (yr)	35.4 ± 10.3	35.9 ± 8.2	35.9 ± 8.2	38.1 ± 9.0	0.085*
PE duration (mo)	34.4 ± 15.1	28.7 ± 15.5	30.5 ± 14.2	36.4 ± 13.4	0.300*

KEY: PE = premature ejaculation.
Data presented as mean ± standard deviation.
* One-way analysis of variance.

specific phosphodiesterase type-5 (PDE-5) inhibitor, which has been used to treat erectile dysfunction. The administration of sildenafil has been found effective for PE treatment in a few studies.^{10,11}

In this study, we compared the efficacy of sildenafil-only, sildenafil plus topical anesthetic cream (EMLA), and topical EMLA-cream-only to placebo for PE treatment.

MATERIAL AND METHODS

The study included 84 patients with PE, whose age ranged from 20 and 52 years at baseline (mean 38.1 ± 9.0). PE was defined as persistent or recurrent ejaculation with minimal sexual stimulation before, at, or shortly after penetration and before the person wished it.¹² All the patients had an active sexual life.

The duration of PE ranged from 9 to 60 months (mean 32.5 ± 14.6). This was the time that the patients consider PE an important sexual problem. The patients underwent a medical and sexual history, including the first five questions of the International Index of Erectile Function, with a detailed physical examination before treatment.

The exclusion criteria were the use of any treatment of PE within the past 2 months, any disease and/or medication that required avoiding sildenafil use, the diagnosis of erectile dysfunction according to the International Index of Erectile Function-5 score (less than 21), decreased libido, alcohol and drug abuse, and the presence of organic or metabolic disorders such as prostatitis, active urinary tract infection, diabetes mellitus, acute or chronic renal failure, and thyroid disease.

After the patients were informed about the efficacy and side effects of the drugs, they were randomized into four groups. Group 1 consisted of 20 patients and took a placebo for 2 months. Groups 2 and 3 consisted of 20 and 22 patients, respectively, and they took 50 mg sildenafil (Viagra) 45 minutes before coitus for 2 months. In addition, patients in group 3 applied topical EMLA cream (lidocaine 2.5%/prilocaine 2.5%) to the glans penis 15 minutes before coitus. The 22 patients in group 4 used topical EMLA-cream-only. The patients did not use a condom during coitus.

After at least eight sexual attempts, the patients' clinical responses were classified as "no change," "improvement," and "cure" according to patient self-report. Cure was defined as ejaculation delayed until patient wished it, and improvement was defined as an increase of ejaculation time compared with the pretreatment time. Effectiveness was described as improvement plus cure. All side effects were recorded.

STATISTICAL ANALYSIS

Statistical analysis was performed with the Statistical Package for Social Sciences for Windows, version 8.0, software. The difference in age was calculated using one-way analysis of variance. Subsequently, the effectiveness of the treatment al-

TABLE II. Clinical responses

Groups	Improvement (%)	Cure (%)	No Change (%)	Total (%)
1	2 (10)	6 (30)	12 (60)	20 (100)
2	4 (20)	7 (35)	9 (45)	20 (100)
3	7 (31.8)	12 (26)	3 (13.6)	22 (100)
4	6 (27.3)	11 (50)	5 (22.7)	22 (100)
Total	19 (22.6)	36 (42.8)	29 (34.6)	84 (100)

ternatives was analyzed using Pearson's correlation test. A P value of less than 0.05 was considered significant.

RESULTS

The patients' age and duration of PE in each group are shown in Table I. No significant differences were observed between patient age and PE duration (one-way analysis of variance, $P = 0.085$ for age and $P = 0.300$ for PE duration).

The clinical responses are given for each group in Table II. The effectiveness was 40% in group 1 (8 of 20), 55% in group 2 (11 of 20), 86.4% in group 3 (19 of 22), and 77.3% in group 4 (17 of 22). A significant difference was found in treatment effectiveness among the four groups (Pearson chi-square = 0.00). No significant difference was found between groups 1 and 2 ($P = 0.26$). Efficiency was more successful in groups 3 and 4 than in the other groups ($P = 0.00$). The difference between groups 3 and 4 was not significant (Pearson chi-square = 0.42; Table II).

Although the patients in groups 1 and 4 did not report any side effects from treatment, headache was observed in 5 (25%) and 6 (27.3%) patients and flushing in 4 (20%) and 7 (31.8%) patients in groups 2 and 3, respectively. However, none of these side effects was severe enough to stop the treatment (Table III).

COMMENT

No consensus has been reached about the definition of PE.⁵ Depending on the study, any ejaculation occurring within 1 to 7 minutes has been considered premature.¹³⁻¹⁶ Others have specified the number of penile thrusts, considering 8 to 15 thrusts as a criterion for PE.¹⁷ These cutoff points

TABLE III. Side effects

Side Effects	Group 1 (n = 20)	Group 2 (n = 20)	Group 3 (n = 22)	Group 4 (n = 22)
Headache	0	5 (25)	6 (27.3)	0
Flushing	0	4 (20)	7 (31.8)	0
Nasal congestion	0	0	0	0
Dyspepsia	0	0	0	0
Visual abnormality	0	0	0	0
Prolonged erection	0	0	0	0
Anejaculation	0	0	0	0

Data presented as number of patients, with percentages in parentheses.

for ejaculation time and thrust number were not derived from objective measurements but were subjectively chosen by the different investigators. The absence of a clear, popular, and widely accepted definition of PE allows a “patient-dependent” definition and a “patient-decided” diagnosis.¹⁸ In the light of published data, we used a patient self-description method for assessing treatment success.

We used the definition of the American Psychiatric Association: PE that is persistent or recurrent ejaculation with minimal sexual stimulation before, at, or shortly after penetration and before the person wished it.¹² Many medical approaches are available, including antidepressants, such as clomipramine, and selective serotonin re-uptake inhibitors, such as paroxetine, sertraline, fluoxetine, and selective and nonselective alpha-1 receptor blockers (phenoxybenzamine, alfuzosin, terazosin), topical anesthetic agents, and PDE-5 inhibitors to treat PE, although none has been sufficient for every patient.^{3,5}

Some recent studies have indicated that PDE-5 inhibitors are effective in the treatment of PE. The efficacy of PDE-5 inhibitors has been suggested to be due to central and peripheral mechanisms. A possible peripheral mechanism includes decreased contractile response on the vas deferens, seminal vesicles, and urethra, peripheral analgesia, and extended erection time. A possible central mechanism is also composed of a decreased delivery of central sympathetic response.^{19,20} Mondaini *et al.*²¹ reported that sildenafil might be used to treat PE by reducing postorgasmic refractory time. Salonia *et al.*¹¹ compared the efficacy of paroxetine alone with that of paroxetine plus sildenafil in a prospective study. They found that combination treatment was superior to paroxetine alone in the treatment of PE. Another study showed that sildenafil ingested as needed as a single treatment for PE increased the ejaculatory latency time more than did paroxetine.¹⁰ Their study found that sildenafil was

superior to all other treatment methods in terms of ejaculatory latency time control and overall satisfaction. A study by McMahon and Samali²² reported finding no significant differences between the sildenafil and placebo groups in terms of intravaginal ejaculatory latency time. Finally, no exact evidence has shown sildenafil success in PE treatment. In our study, no significant difference was found between the sildenafil-only group and the placebo group. In the placebo group, the success rate was 40%. We could not explain the high success rate in the placebo group. Our results indicated that sildenafil-only was an ineffective treatment option for PE. Furthermore, sildenafil did not augment the topical anesthetic cream’s efficacy. In the present study, the combination of sildenafil and topical anesthetic cream had similar efficacy in PE treatment. A larger patient sample and placebo-controlled study in men with PE are needed to confirm our results.

An experimental study showed that application of topical anesthetics to the penis virtually abolished the display of penile reflexes in rats.²³ This has also been confirmed in a clinical study.⁴ Berkovitch *et al.*²⁴ reported that local anesthesia with prilocaine-lidocaine cream applied to the penile skin delayed ejaculation. Another study showed that topical lidocaine-prilocaine spray administration to the glans penis led to eight times increased intravaginal ejaculation latency time and improved sexual satisfaction in patients and their partners.²⁵ Atikeler *et al.*,⁹ documented that topical prilocaine-lidocaine cream application significantly provided improved intravaginal ejaculation time compared with placebo. In the present study, the topical EMLA cream plus sildenafil group and the topical EMLA-cream-only group were superior to the placebo and sildenafil-only groups. However, topical EMLA-cream-only was as effective as topical EMLA cream plus sildenafil. Hence, we concluded that topical EMLA-cream-only treatment is sufficient to delay ejaculation.

The problems in using topical local anesthetics in the treatment of PE are significant penile hypoesthesia and vaginal numbness due to possible transvaginal absorption. They may cause male and female anorgasmia. However, these have not been seen in all patients.³ Topical anesthetics are only contraindicated for patients and/or their partners with allergies to any component of the product.^{3,18} In our study, no patient described anorgasmia due to penile hypoesthesia. However, we do not know whether female anorgasmia occurred in our study, because the patients’ partners were not evaluated after treatment. This was a weak point of our study. Also, partner satisfaction was not considered in this study.

CONCLUSIONS

Although some studies have reported sildenafil success for PE, in the present study, sildenafil-only was not a more effective treatment option than placebo. Although the sildenafil plus topical EMLA cream and topical EMLA-cream-only treatments were superior to placebo and sildenafil-only treatment of PE, topical EMLA cream alone had effectiveness equal to that of the combination treatment. Hence, topical EMLA cream alone seems a reasonable, inexpensive, and effective treatment modality for PE treatment.

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