

Efficacy of Local Agents Used in Premature Ejaculation Treatment

Mustafa hamarat

mustafabilal.hamarat@sbu.edu.tr

University of Health Sciences <https://orcid.org/0000-0002-3987-7016>

alper kafkaslı

kartal eğitim ve araştırma hastanesi

onur kucuktopcu

Berk Karatas

Article

Keywords: Premature Ejaculation, Local Treatment, Intravaginal Ejaculation Latency Time

Posted Date: March 15th, 2024

DOI: <https://doi.org/10.21203/rs.3.rs-4006624/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: There is **NO** conflict of interest to disclose.

Abstract

Premature ejaculation is a common sexual dysfunction in men. Some topical anesthetic agents are used in the treatment to reduce the hypersensitivity of the glans. The number of patients in studies showing the effectiveness of topical agents is limited. This study aimed to evaluate the effects of a eutectic mixture of lidocaine and prilocaine-containing local anesthetic creams (EMLA), lidocaine spray, and benzocaine condoms on ejaculation, which are widely used in Turkey in premature ejaculation patients. Between November 2020 and December 2022, 273 male patients who were admitted to the andrology polyclinic of the hospital and diagnosed with PE for life were included in the study. Age, body mass index, marriage periods, intercourse durations, relationship frequency, comorbidities, duration of intravaginal ejaculation latency time (IELT) before and 2 months after treatment and side effects of the patients after treatment were prospectively collected. Patients were divided into 3 groups. Group 1 consisted of patients using EMLA cream, respectively; group 2 consisted of patients using lidocaine spray, and group 3 consisted of patients using benzocaine condoms. 59 people in group 1, 126 in group 2, and 88 in group 3 were included in the study. Pre-treatment IELT values of Groups 1, 2, and 3 were 32.5 ± 17.7 sec, 29.8 ± 17.9 sec, and 30.1 ± 13.9 s, respectively. Post-treatment IELT values were 104.5 ± 135.81 sec, 144.1 ± 179.8 sec, and 75.1 ± 50.4 s, respectively. In all three groups, post-treatment IELT values were significantly higher than before treatment. Our study found that spray and EMLA cream significantly increased IELT duration compared to condoms. Although local treatments used in premature ejaculation are effective in the short term, further studies showing long-term efficacy are needed.

INTRODUCTION

Premature ejaculation (PE) is the most common sexual dysfunction in men characterized by the inability to delay orgasm and ejaculation.^{1, 2} In a study conducted in the United States, the prevalence of PE in men between the ages of 18–59 was found to be 31%.³ In addition to the inability to delay ejaculation in patients, PE can cause negative personal consequences such as avoidance of sexual intimacy and frustration. In 2014, the International Society of Sexual Medicine (ISSM) defined lifelong PE and acquired PE and stated that PE patients should be evaluated in two separate groups. Lifetime PE is characterized by ejaculation that occurs before or within 1 minute of vaginal penetration from the first sexual experience, while acquired PE is characterized by ejaculation that occurs later and occurs before or within 3 minutes after vaginal penetration.⁴

Psychological and biological factors have been implicated in the etiology of premature ejaculation. Accordingly, pharmacological and behavioral therapies are applied in the treatment.⁵ One of the biological factors suggested is the increase in the sensitivity of the glans penis.⁶ Some topical anesthetic agents are used in the treatment to reduce the hypersensitivity of the glans. In this regard, various products containing lidocaine or prilocaine are used in the treatment.⁷ Another product commonly used among patients is retardant condoms, which also contain lidocaine or benzocaine.⁷ In this study, we aimed to evaluate the effects of an eutectic mixture of local anesthetic creams containing

lidocaine and prilocaine (EMLA), lidocaine spray and benzocaine condom on ejaculation in premature ejaculation patients.

MATERIAL AND METHOD

Study design

Between November 2020 and December 2022 heterosexual patients who had intercourse at least once a week, had intercourse with their partner for more than 3 months, had a baseline IELT $\leq$ of 60 seconds, and were diagnosed with lifelong PE according to ISSM criteria were included in the study. The time from the entry of the penis into the vagina to intravaginal ejaculation was defined as IELT. Patients who were or wanted to use oral therapy or combination therapy were excluded from the study. The patients who came to the Andrology outpatient clinic were told about the local treatments using EMLA cream containing 2.5% lidocaine and 2.5% prilocaine, spray containing 10% lidocaine and condom, and the treatment requested by the patient was started. Patients' age, body mass index, duration of marriage, duration of intercourse, frequency of intercourse, comorbidities, duration of treatment and 2 months after treatment, and side effects of patients and their partners after treatment were collected prospectively. The patients were divided into 3 groups. Patients using EMLA cream in group 1, respectively; Group 2 consisted of patients using lidocaine spray and group 3 consisted of patients using condoms.

In group 1, 2.5 g of EMLA cream was applied to the penis 20–30 minutes before intercourse, and then a condom was used to cover it. Just before vaginal penetration, the condom was removed, the penis was cleaned and intercourse was performed. In group 2, 10 minutes before intercourse, the penis was sprayed with lidocaine spray, then a condom was used, after 10 minutes, the condom was removed and intercourse was started. In group 3, patients used condoms before intercourse and had intercourse.

Patients with diabetes mellitus, patients with genitourinary tract infection, patients with psychiatric illness and drug use, and patients who received treatment for erectile dysfunction or PE in the last 1 month were excluded from the study. At 2 months, patients were evaluated on an outpatient basis, by phone or online. Patients who were evaluated at 2 months and had IELT values before and after treatment were analyzed. The primary outcome of our study was the change in IELT values after treatment. Comparison of adverse reactions and intergroup IELT changes were secondary results.

Statistical analyses

Statistical analyses of the values were carried out using SPSS (Statistical Package for Social Sciences) 22.0 statistical software package. Chi-square test was used to compare numbers in statistical analysis, the Wilcoxon test was one of the nonparametric tests since all data showed heterogeneous distribution in comparison of averages, and the Tamhane technique was preferred in post hoc analysis in the ANOVA test.

Ethical committee approval

The study was conducted by the Declaration of Helsinki and Good Clinical Practice. Ethics committee approval of this study was obtained from the ethics committee of Dr. Lütfi Kırdar Kartal City Hospital.

RESULTS

A total of 273 people who were diagnosed with lifetime PE and met the criteria mentioned above were included in the study. 59 people in group 1, 126 in group 2 and 88 in group 3 were included in the study. The mean IELT values of groups 1, 2 and 3 were 32.5 + 17.7 sec, 29.8 + 17.9 sec and 30.1 + 13.9 sec, respectively. The post-treatment values were 104.5 + 135.81 sec, 144.1 + 179.8 sec and 75.1 + 50.4 sec, respectively. In all three groups, post-treatment IELT values were significantly higher than before treatment (Table 1).

Table 1
IELT scores before and after treatment in treatment groups

	IELT score before treatment (sec)	IELT score after treatment (sec)	P-value
Group 1 (Cream)	32,5 + 17,7	104,5 + 135,81	< 0.05
Group 2 (Spray)	29,8 + 17,9	144,1 + 179,8	< 0.05
Group 3 (Condom)	30,1 + 13,9	75,1 + 50,4	< 0.05
Wilcoxon test, which is a non-parametric test, was used because the values before and after IELT were heterogeneously distributed.			

There was no significant difference between body mass index, age, duration of intercourse, frequency of weekly sexual intercourse and pre-treatment IELT scores in the demographic data of the patients (Table 2).

Table 2
Demographic data of patients

	Groups			
	Group 1 (Cream)	Group 2 (Spray)	Group 3 (Condom)	P-value
Number of patients	59	126	88	
Body mass index (kg/m ²)	26,6 + 3,5	26,1 + 3,7	25,3 + 3,1	0,071
Age (years)	34,6 + 8,2	33,1 + 7,2	33,5 + 9,5	0,542
Duration of marriage (years)	6,6 + 7,3	5,7 + 6,7	6,0 + 7,9	0,767
Pre-treatment IELT score (sec)	32,5 + 17,7	29,8 + 17,9	30,1 + 13,9	0,581
Since body mass index, age, duration of marriage and pre-treatment IELT score were heterogeneously distributed, Tamhane test was selected as the post Hoc test in the ONE WAY ANOVA test and compared.				

According to the ANOVA tests the mean increase in IELT score was found to be higher in group 2 than in group 1 and group 3, and while this increase was not statistically significant compared to group 1, it was statistically significant compared to group 3 ($p = 0.203$ and $p < 0.05$) (Table 3). The mean increase in IELT score between group 1 and group 3 was not statistically significant ($p = 0.356$).

Table 3
Evaluation of treatment outcomes

	Groups			
	Group 1 (Cream)	Group 2 (Spray)	Group 3 (Condom)	P-value
Mean increase in IELT score (sec)	72,0 + 131,9	114,3 + 178,9	44,9 + 48,9	0,001

When the side effects of the treatment were compared, no systemic side effects were observed in all three groups. Side effects were observed in a total of 12 patients (20.3%) in group 1, 18 patients (14.2%) in group 2 and 6 patients (6.8%) in group 3. The number of patients with side effects was lower in group 3 compared to the other groups and this was statistically significant ($p:0.015$). Erectile dysfunction was observed in 8 (12%) of the patients in group 1, 10 patients (7.9%) in group 2 and 3 patients (3.4%) in group 3 and this rate was significantly higher in group 1 ($p:0.023$). Local side effects (burning, difficulty in intercourse, numbness, etc.) were observed in the partners of 12.6% of the patients in group 2, and this rate was significantly higher compared to the other groups ($p:0.048$) (Table 4).

Table 4
Assessment of side effects

	Groups			P-value
	Group 1 (Cream)	Group 2 (Spray)	Group 3 (Condom)	
Side effects	12 (20.3%)	18 (14.2%)	6 (6.8%)	0.015
Erectile dysfunction	8 (13%)	10 (7.9%)	3 (3.4%)	0.023
Local side effects on female partner	4 (6.7%)	16 (12.6%)	3 (3.4%)	0.048

DISCUSSION

The long-term use of SSRIs, one of the oral agents used in the treatment of PE, is very low due to various side effects.⁸ This situation increases the importance of local anesthetic agents in the treatment of PE. Local anesthetic agents act by reducing increased hypersensitivity in the glans penis, which plays a role in the etiology of premature ejaculation.⁹ In our study, 273 patients were evaluated. We observed that eutectic mixture of local anesthetics, lidocaine spray and benzocaine condom, which are frequently used in our country, are effective in the treatment of PE. In addition, we observed that the treatment efficacy of lidocaine spray and lidocaine-prilocaine cream was significantly higher than benzocaine condoms. We observed that the side effects of the treatment were significantly lower in patients using condoms compared to other groups.

In a study by Dell'Atti et al., patients with PE were divided into 3 groups: the first group was given topical lidocaine spray 10%, the second group was given 5 mg of tadalafil daily, and the third group was given these two treatments together. While there was a significant increase in IELT values in all three groups compared to the baseline, the mean IELT result at the beginning of 25 patients in the group given only lidocaine was 1.1 ± 0.3 minutes, while this value was 3.7 ± 1.3 minutes at the end of the 3rd month ($p < 0.001$).¹⁰ In a study conducted by Alghobary et al., the mean initial IELT result of 55 patients with premature ejaculation was 21.87 seconds, while this value was 179.43 seconds after topical 10% lidocaine spray treatment. In the same study, 43 (78.2%) of the patients found topical lidocaine treatment to be effective.¹¹ In the study conducted by El-Hamd, 75 patients who used 5% lidocaine spray for the treatment of PE had an average of 0.60 minutes before the treatment, while this value was 6.26 minutes after the treatment.¹² In our study, the mean IELT value was 29.8 sec in the spray group before treatment and 144.1 sec after treatment. In our study, the results in the spray group were similar to the results of the study of Alghobary et al. In the other studies mentioned, the mean IELT values after treatment were higher than in our study. In other studies, patients were usually evaluated at 3 months after the start of treatment, while in our study, they were evaluated at 2 months. This may have affected the results.

Dinsmore and Wyllie; In a study using a spray consisting of an aerosol formulation of 7.5 mg of lidocaine and 2.5 mg of prilocoine, they found that the average IELTS in 191 PE patients increased from 0.6 minutes to 3.8 minutes after 3 months of treatment.¹³ Busato and Galindo found that in 24 patients using EMLA cream, the mean IELT was 1.49 minutes before treatment and 8.45 minutes after treatment.¹⁴ In our study, 58 patients who used EMLA cream had an IELT of 32.5 seconds before treatment and 104.5 seconds after treatment. In our study, although the increase in mean IELT values after treatment was relatively low compared to other studies, it was significantly higher than before treatment.

In a study conducted by Wang et al., the effects of a condom thickened 3 times more than a normal-thickness condom on the duration of ejaculation latency in patients with premature ejaculation were evaluated. It was found that the ejaculation latency time was significantly prolonged after the use of thickened condoms in patients with premature ejaculation.¹⁵ In a prevalence study conducted by Waldinger et al., premature ejaculation rates, IELT times and condom use were evaluated in men in the five countries included in the study. In the study, in which approximately 500 patients were evaluated, it was determined that 29% of the patients used condoms. The mean IELT value of the patients using condoms was 5.7 minutes, while the IELT value of the patients who did not use it was 5.1 minutes, and there was no significant difference between the two groups.¹⁶ In our study, the average IELT value of the patients before using condoms was 30.1 + 13.9 sec and this value was 75.1 + 50.4 sec after condom use, and a statistically significant increase was found ($p < 0.05$).

In their study, Alghobary et al. reported a decrease in erection that did not interfere with intercourse in 61.8% of patients treated with topical lidocaine, while glans penile irritation was reported in 4 patients (7.3%).¹¹ In a study using Fortaci, an aerosol containing 150 mg/mL lidocaine and 50 mg/mL prilocoine, they observed side effects such as genital burning sensation (7.0%), bothersome local hypoesthesia (3.9%) and erectile dysfunction (2.3%).¹⁷ In the study conducted by Dell'Atti et al., genital burning sensation was detected in 4%, genital erythema in 4%, and hypoesthesia in the penis in 8% of the group using topical lidocaine spray 10%.¹⁰ Busato and Galindo reported a burning sensation in the penis in 2 (8.3%) of 24 patients using EMLA cream, delayed ejaculation in 2 (8.3%), and decreased vaginal sensitivity in 1 (4.2%) patient's partner.¹⁴ In our study, side effects such as local hypoesthesia, erectile dysfunction, burning of the penis and discomfort in the partner were observed. Similar to the literature, no systemic side effects were observed in any of the patients. While side effects were observed in the cream and spray group similar to the literature, the side effects observed in the cream and spray group were statistically significantly higher than in the preservative group. While the side effects observed in the female partner were significantly higher in the spray group than in the cream group, the rate of erectile dysfunction was also significantly higher in the cream group.

The fact that no evaluation criterion for premature ejaculation was used in patients is an important limitation of the study. In addition, the lack of long-term outcomes of the patients was one of the

important limitations. Despite these limitations, our study has a very high number of patients among the prospective studies on topical treatments to date.

CONCLUSION

In our study, we found that the eutectic mixture of local anesthetic creams containing lidocaine and prilocaine, lidocaine spray and benzocaine condom, which are frequently used in premature ejaculation in Turkey, statistically significantly increased IELT times compared to baseline. In particular, we found that spray and EMLA cream significantly increased IELT time compared to condoms. Although local treatments used in premature ejaculation are effective in the short term, further studies showing their long-term effectiveness are needed.

Declarations

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Martin C, Nolen H, Podolnick J, Wang R. Current and emerging therapies in premature ejaculation: Where we are coming from, where we are going. *Int J Urol*. Jan 2017;24(1):40-50.
2. McCabe MP, Sharlip ID, Lewis R, et al. Incidence and Prevalence of Sexual Dysfunction in Women and Men: A Consensus Statement from the Fourth International Consultation on Sexual Medicine 2015. *J Sex Med*. Feb 2016;13(2):144-152.
3. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *Jama*. Feb 10 1999;281(6):537-544.
4. Porst H, Burri A. Novel Treatment for Premature Ejaculation in the Light of Currently Used Therapies: A Review. *Sex Med Rev*. Jan 2019;7(1):129-140.
5. Castiglione F, Albersen M, Hedlund P, Gratzke C, Salonia A, Giuliano F. Current Pharmacological Management of Premature Ejaculation: A Systematic Review and Meta-analysis. *Eur Urol*. May 2016;69(5):904-916.
6. Guo L, Liu Y, Wang X, et al. Significance of penile hypersensitivity in premature ejaculation. *Sci Rep*. Sep 5 2017;7(1):10441.
7. Raveendran AV, Agarwal A. Premature ejaculation - current concepts in the management: A narrative review. *Int J Reprod Biomed*. Jan 2021;19(1):5-22.
8. Jenkins LC, Gonzalez J, Tal R, Guhring P, Parker M, Mulhall JP. Compliance With Fluoxetine Use in Men With Primary Premature Ejaculation. *J Sex Med*. Dec 2019;16(12):1895-1899.
9. Wyllie MG, Hellstrom WJ. The link between penile hypersensitivity and premature ejaculation. *BJU Int*. Feb 2011;107(3):452-457.

10. Dell'Atti L, Galosi A, Ippolito CJERMPS. A randomized single-center study to compare the efficacy and tolerability of tadalafil once daily plus lidocaine anesthetic spray on premature ejaculation. 2017;21(5):1036-1040.
11. Alghobary M, Gaballah M, El-Kamel MF, et al. Oral dapoxetine versus topical lidocaine as on-demand treatment for lifelong premature ejaculation: A randomised controlled trial. *Andrologia*. Jun 2020;52(5):e13558.
12. Abu El-Hamd M. Effectiveness and tolerability of lidocaine 5% spray in the treatment of lifelong premature ejaculation patients: a randomized single-blind placebo-controlled clinical trial. *Int J Impot Res*. Jan 2021;33(1):96-101.
13. Dinsmore WW, Wyllie MG. PSD502 improves ejaculatory latency, control and sexual satisfaction when applied topically 5 min before intercourse in men with premature ejaculation: results of a phase III, multicentre, double-blind, placebo-controlled study. *BJU Int*. Apr 2009;103(7):940-949.
14. Busato W, Galindo CC. Topical anaesthetic use for treating premature ejaculation: a double-blind, randomized, placebo-controlled study. *BJU Int*. May 2004;93(7):1018-1021.
15. Wang Z, Yu J. Efficacy evaluation of thickened condom in the treatment of premature ejaculation. *Transl Androl Urol*. Feb 2022;11(2):253-259.
16. Waldinger MD, Quinn P, Dilleen M, Mundayat R, Schweitzer DH, Boolell M. ORIGINAL RESEARCH—EJACULATION DISORDERS: A Multinational Population Survey of Intravaginal Ejaculation Latency Time. *The Journal of Sexual Medicine*. 2005/07/01/ 2005;2(4):492-497.
17. Boeri L, Pozzi E, Fallara G, Montorsi F, Salonia A. Real-life use of the eutectic mixture lidocaine/prilocaine spray in men with premature ejaculation. *Int J Impot Res*. Apr 2022;34(3):289-294.