The Analysis Study of Efficacy and Safety of Topical Anesthetic Agent for Treatment of Premature Ejaculation: A Comprehensive Systematic Review

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Article History:
Received date: 2023/12/03
Revised date: 2024/03/12
Accepted date: 2024/04/22
Published date: 2024/07/30

ABSTRACT

Background: Premature ejaculation (PE) affects 20-30% of men globally, with lifelong and acquired types requiring diverse behavioral and pharmacological treatments. This systematic review aims to analyze current evidence on the efficacy and safety of topical anesthetic agent for treatment of premature ejaculation based on literatures of the last 10 years.

Methods: The study adhered to PRISMA 2020 standards, examining English literature from 2014 to 2024. PubMed, SagePub, SpringerLink, and Google Scholar were utilized as literature sources. Result: Initially retrieving 360 articles from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) six relevant papers were selected after three rounds of screening for full-text analysis.

Conclusion: Overall, the evidence suggests that topical anesthetic agents are effective in treating PE. These agents consistently improve IELT and patient satisfaction, with a favorable safety profile. The findings also highlight the importance of individualized treatment approaches, considering patient preferences, sexual habits, and the specific characteristics of PE.

Keyword: topical anesthetic, premature ejaculation, efficacy, safety
INTRODUCTION

Premature ejaculation (PE) is the most prevalent male sexual dysfunction, impacting approximately 20-30% of men globally.¹ This condition is characterized by a short ejaculatory latency and a perceived lack of control over ejaculation, which often leads to significant distress and interpersonal difficulties. Men suffering from PE may experience mental anguish, anxiety, shame, and depression, all of which can harm their self-esteem and strain their relationships with partners. The wide-reaching effects of PE highlight the importance of a clear understanding and effective management of the condition.²

PE can be classified into two main types: lifelong (primary) and acquired (secondary). Lifelong PE begins at sexual maturity and persists throughout a man’s life, whereas acquired PE develops after a period of normal sexual function. The International Society for Sexual Medicine (ISSM) defines PE as a male sexual dysfunction characterized by ejaculation occurring either before or within 60 seconds of vaginal penetration in cases of lifelong PE, or within three minutes in cases of secondary PE. Additionally, PE is marked by an inability to delay ejaculation in nearly all vaginal penetrations and negative personal consequences such as stress, dissatisfaction, and avoidance of sexual intimacy.³,⁴

Treatment for PE aims to alleviate the distress associated with the condition and improve sexual satisfaction for both the patient and their partner. A variety of treatment options are available, including both behavioral and pharmacological interventions. Behavioral techniques may involve exercises to improve ejaculatory control and reduce performance anxiety.⁵ Pharmacological treatments include the use of selective serotonin reuptake inhibitors (SSRIs) and local anesthetics. Local anesthetics, such as the topical lidocaine–prilocaine cream recommended by the European
Association of Urology, work by reducing the sensitivity of the glans penis, thereby delaying ejaculation without adversely affecting the sensation of ejaculation.\textsuperscript{6,7}

Despite the availability of various treatment options, systematic reviews and meta-analyses of treatments for PE have faced significant challenges. These include issues such as missing data and inconsistencies in the outcome measures reported across randomized controlled trials (RCTs). Such challenges complicate the process of pooling data and drawing robust conclusions about the efficacy of different treatments.\textsuperscript{8} Consequently, there is a need for more standardized and comprehensive reporting in future studies to ensure that the evidence base for PE treatments is as reliable and informative as possible.

This systematic review aims to analyze current evidence on the efficacy and safety of topical anesthetic agent for treatment of premature ejaculation based on literatures of the last 10 years.

\section*{METHODS}

\subsection*{Protocol}

The author carefully followed the rules laid out in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This was done to make sure the study met all its standards. The selection of this methodological approach was specifically aimed at ensuring the precision and reliability of the conclusions drawn from the investigation.

\subsection*{Criteria for Eligibility}

This systematic review investigate existing evidence on the efficacy and safety of topical anesthetic agent for treatment of premature ejaculation based on literatures of the last 10 years. This study meticulously analyzed data on literatures to provide insights and enhance patient treatment strategies. The primary objective of this paper is to highlight the collective significance of the identified key points.

Inclusion criteria for this study entail: 1) Papers must be in
English, and 2) Papers must have been published between 2014 and 2024. Exclusion criteria comprise: 1) Editorials; 2) Submissions without a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

**Search Strategy**

The keywords used for this research are acute kidney injury, chronic kidney disease, prevalence, incidence. The Boolean MeSH keywords inputted on databases for this research are: "anesthetics local"[Pharmacological Action] OR "anesthetics, local"[MeSH Terms] OR "anesthetics"[All Fields] AND "local"[All Fields] OR "local anesthetics"[All Fields] OR "topical"[All Fields] AND "anesthetic"[All Fields] OR "topical anesthetic"[All Fields]) AND ("premature ejaculation"[MeSH Terms] OR "premature"[All Fields] AND "ejaculation"[All Fields]) OR "premature ejaculation"[All Fields]) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields]) AND ("safety"[MeSH Terms] OR "safety"[All Fields] OR "safeties"[All Fields]) AND (y_10[Filter])

**Data retrieval**

The authors assessed the studies by reviewing their abstracts and titles to determine their eligibility, selecting relevant ones based on their adherence to the inclusion criteria, which aligned with the article's objectives. A consistent trend observed across multiple studies led to a conclusive result. The chosen submissions had to meet the eligibility criteria of being in English and a full-text.

This systematic review exclusively incorporated literature that met all predefined inclusion criteria and directly pertained to the investigated topic. Studies failing to meet these criteria were systematically excluded, and their findings were not considered. Subsequent analysis examined various details uncovered during the research process, including titles, authors, publication dates, locations, study methodologies, and parameters.
Quality Assessment and Data Synthesis

Each author independently evaluated the research presented in the title and abstract of the publication to determine which ones merited further exploration. The subsequent stage involved assessing all articles that met the predefined criteria for inclusion in the review. Decisions on including articles in the review were based on the findings uncovered during this evaluation process.

**Figure 1. Article search flowchart**

The International Journal of Medical Science and Health Research
RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 360 articles. After conducting three levels of screening, six articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 1 presents the selected literature included in this analysis.

Dell'Atti, et al.\(^9\) (2017) showed that daily tadalafil is effective in treating lifelong PE, and its efficacy is significantly enhanced when combined with lidocaine spray before intercourse, as indicated by the increased mean IELT.

El-Hamd, et al.\(^{10}\) (2021) showed that applying lidocaine 5% spray to the glans penis 10–20 minutes before intercourse significantly improves PE symptoms with tolerable local adverse effects.

Alghobary, et al.\(^{11}\) (2020) showed that topical lidocaine is a more effective on-demand therapy for lifelong PE compared to oral dapoxetine.

Gameel, et al.\(^{12}\) (2014) showed that topical anesthetic lidocaine and other drugs significantly improved IELT values compared to placebo and had tolerable side effects. Tramadol provided the longest IELT, while sildenafil offered the highest improvement in sexual satisfaction.

Boeri, et al.\(^{13}\) (2021) showed that prilocaine/lidocaine spray was found to be a safe and effective treatment for various types of PE, with almost one-fourth of patients still using it after 12 months. Timing and dosing adjustments may be necessary based on individual needs and sexual habits.

Shabsigh, et al.\(^{14}\) (2017) showed that benzocaine wipes applied topically to the penis before intercourse significantly prolonged time to ejaculation, providing a clinically meaningful benefit in treating premature ejaculation. Benzocaine wipes were well tolerated and did not transfer to female partners.
## Table 1. The literature included in this study

<table>
<thead>
<tr>
<th>No.</th>
<th>Author</th>
<th>Origin</th>
<th>Method</th>
<th>Sample</th>
<th>Result</th>
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<tbody>
<tr>
<td>1.</td>
<td>Dell'Atti, et al.⁹ (2017)</td>
<td>Italy</td>
<td>Randomized controlled trial</td>
<td>78 patients</td>
<td>The study involved 78 men in stable heterosexual, monogamous relationships (≥3 months) diagnosed with lifelong PE. They were divided into three groups: G1 (25 patients) received lidocaine spray 10 g/100 ml 5 minutes before intercourse, G2 (27 patients) received tadalafil 5 mg daily, and G3 (26 patients) received tadalafil daily plus lidocaine spray before planned sexual activity. Treatments lasted three months, and sexual quality was rated on a 5-point scale, with follow-ups at one and three months. Results showed no significant differences between groups at baseline. At the three-month follow-up, mean ejaculatory latency times were 3.7±1.3 minutes for G1, 3.4±1.5 minutes for G2, and 5.6±1.7 minutes for G3 (p&lt;0.001). Mean satisfaction scores at three months were 2.8±1.4 for G1, 2.9±1.8 for G2, and 3.7±1.5 for G3 (p&lt;0.002). No patients withdrew due to adverse events.</td>
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<td>2.</td>
<td>El-Hamd, et al.¹⁰ (2021)</td>
<td>Egypt</td>
<td>Randomized controlled trial</td>
<td>150 patients</td>
<td>This randomized single-blind placebo-controlled clinical trial involved 150 patients with lifelong PE and normal erections. The patients were evenly divided into two groups: Group 1 (75 patients) received on-demand lidocaine 5% spray for 8 weeks, and Group 2 (75 patients) received a placebo alcohol spray for 8 weeks. Both treatments were applied to the glans penis 10–20 minutes before intercourse and then cleaned off before planned sexual activity. Patients were assessed using the Arabic Index of Premature Ejaculation (AIPE) scores, intravaginal ejaculatory latency times (IELTs), and frequency of sexual intercourse before...</td>
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and after treatment. Results showed that the lidocaine 5% spray group had statistically significant improvements in AIPE scores, IELTs, and frequency of sexual intercourse compared to the placebo group (P = 0.0001).

The results showed that both topical lidocaine and oral dapoxetine significantly increased intravaginal ejaculatory latency times (IELT) and Arabic Index of Premature Ejaculation (AIPE) scores compared to baseline. Topical lidocaine had a more substantial effect, with IELT increasing to 179.4 seconds from 63.44 seconds, compared to 21.87 seconds for dapoxetine (p < .05). However, a significant decrease in the Sexual Health Inventory for Men (SHIM) score was observed with lidocaine but not with dapoxetine. The Global Efficacy Question revealed that 43 patients found lidocaine effective and 12 ineffective, while 16 found dapoxetine effective and 39 ineffective.

The study found that tramadol-treated patients had the longest mean intravaginal ejaculatory latency time (IELT) of 351 seconds, significantly longer than other groups. Local anesthetic was more effective than paroxetine in prolonging IELT, with mean times of 278 seconds versus 186 seconds, respectively. Sildenafil showed the greatest improvement in sexual satisfaction, with a mean increase of 2.9 points, compared to 2.2 points for paroxetine and 1.9 points for local anesthetic.

The study included 198 men with a mean age of 37 years, reporting lifelong PE (51%), acquired PE (29.8%), and subjective PE (19.2%) at baseline. prilocaine/lidocaine spray use

<table>
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<tr>
<th>Study</th>
<th>Authors</th>
<th>Country</th>
<th>Study Design</th>
<th>Number of Patients</th>
<th>Findings</th>
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</thead>
<tbody>
<tr>
<td>3.</td>
<td>Alghobary, et al.11 (2020)</td>
<td>Egypt</td>
<td>Randomised controlled trial</td>
<td>55 patients</td>
<td>The results showed that both topical lidocaine and oral dapoxetine significantly increased intravaginal ejaculatory latency times (IELT) and Arabic Index of Premature Ejaculation (AIPE) scores compared to baseline. Topical lidocaine had a more substantial effect, with IELT increasing to 179.4 seconds from 63.44 seconds, compared to 21.87 seconds for dapoxetine (p &lt; .05). However, a significant decrease in the Sexual Health Inventory for Men (SHIM) score was observed with lidocaine but not with dapoxetine. The Global Efficacy Question revealed that 43 patients found lidocaine effective and 12 ineffective, while 16 found dapoxetine effective and 39 ineffective.</td>
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<td>4.</td>
<td>Gameel, et al.12 (2014)</td>
<td>Egypt</td>
<td>Randomised controlled trial</td>
<td>150 patients</td>
<td>The study found that tramadol-treated patients had the longest mean intravaginal ejaculatory latency time (IELT) of 351 seconds, significantly longer than other groups. Local anesthetic was more effective than paroxetine in prolonging IELT, with mean times of 278 seconds versus 186 seconds, respectively. Sildenafil showed the greatest improvement in sexual satisfaction, with a mean increase of 2.9 points, compared to 2.2 points for paroxetine and 1.9 points for local anesthetic.</td>
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<td>5.</td>
<td>Boeri, et al.13 (2021)</td>
<td>Italy</td>
<td>Retrospective cohort</td>
<td>198 patients</td>
<td>The study included 198 men with a mean age of 37 years, reporting lifelong PE (51%), acquired PE (29.8%), and subjective PE (19.2%) at baseline. prilocaine/lidocaine spray use</td>
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increased over six months, with 92.9% having tried it and 66.4% regularly using it. At the 12-month follow-up, 26.8% continued regular use. The mean Premature Ejaculation Diagnostic Tool score significantly decreased at 6 and 12 months compared to baseline ($p < 0.05$), and the mean intravaginal ejaculatory latency time (IELT) significantly improved at 6 months ($p \leq 0.04$).

<table>
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<tr>
<th>6.</th>
<th>Shabsigh, et al.(^{14}) (2017) USA</th>
<th>Randomized controlled trial</th>
<th>21 patients</th>
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<tbody>
<tr>
<td>The study showed that the treatment group using benzocaine wipes had a statistically significant increase in intravaginal ejaculatory latency time (IELT) compared to the placebo group. At the treatment phase baseline, the treatment group had a mean IELT of 165 seconds versus 110 seconds for the placebo group ($P&lt;0.007$). After two months, the treatment group's mean IELT increased to 329.70 seconds compared to 110.10 seconds in the placebo group ($P=0.001$). In the open-label phase, further increases in IELT were observed in the treatment group, and a significant increase was seen in the placebo/crossover group. Using the Index of Premature Ejaculation (IPE), men in the treatment group reported significantly higher sexual satisfaction ($P=0.047$) and greater improvement in distress ($P=0.020$), with a trend towards better ejaculatory control ($P=0.093$). The responder analysis confirmed a clinically meaningful IELT increase with benzocaine versus placebo. Benzocaine wipes were well tolerated by both subjects and their partners, with no evidence of transference.</td>
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</table>
The efficacy and safety of topical anesthetic agents for the treatment of premature ejaculation (PE) have been investigated in various clinical trials, demonstrating promising results. Dell'Atti et al. (2017) conducted a randomized controlled trial with 78 men in stable heterosexual relationships, diagnosed with lifelong PE. The study found that daily tadalafil, particularly when combined with lidocaine spray before intercourse, significantly improved intravaginal ejaculatory latency times (IELT) and sexual satisfaction. This combination therapy yielded mean IELT values of 5.6±1.7 minutes, suggesting enhanced efficacy compared to either treatment alone.

El-Hamd et al. (2021) explored the use of lidocaine 5% spray in a randomized, single-blind, placebo-controlled trial involving 150 patients with lifelong PE. The study found that applying lidocaine 5% spray to the glans penis 10–20 minutes before intercourse significantly improved PE symptoms, including IELT, AIPE scores, and frequency of sexual intercourse, compared to the placebo group. The findings indicated that lidocaine 5% spray is both effective and tolerable for PE treatment, offering a non-invasive therapeutic option.

Alghobary et al. (2020) compared topical lidocaine with oral dapoxetine in a randomized controlled trial involving 55 patients. The study found that topical lidocaine significantly increased IELT and AIPE scores more than oral dapoxetine. The treatment also resulted in higher patient satisfaction, with 43 patients finding lidocaine effective compared to 16 for dapoxetine. These results support the use of topical lidocaine as a more effective on-demand therapy for lifelong PE.

Gameel et al. (2014) assessed the efficacy of tramadol, local anesthetics, and other drugs in a randomized controlled trial with 150 patients. Tramadol-treated patients had the longest mean IELT (351 seconds), while local anesthetics showed better results than paroxetine (278 seconds vs. 186 seconds). Sildenafil provided the greatest improvement in sexual satisfaction.
These findings indicate that while multiple treatments can be effective, tramadol and local anesthetics are particularly potent in prolonging IELT.\textsuperscript{17}

Boeri et al. (2021) conducted a retrospective cohort study with 198 men, evaluating the long-term use of prilocaine/lidocaine spray. The study showed significant decreases in the Premature Ejaculation Diagnostic Tool scores and improvements in IELT at both 6 and 12 months. Despite the decline in regular use over time, almost one-fourth of patients continued using the spray after 12 months, highlighting its long-term efficacy and safety.\textsuperscript{13} The need for timing and dosing adjustments based on individual sexual habits was also emphasized.\textsuperscript{18}

Shabsigh et al. (2017) investigated benzocaine wipes in a randomized, placebo-controlled trial with 21 patients. The study demonstrated a significant increase in IELT and higher sexual satisfaction and reduced distress in the treatment group compared to the placebo group.\textsuperscript{14} Benzocaine wipes were well tolerated by both subjects and their partners, with no evidence of transference, making them a viable option for PE treatment.\textsuperscript{19}

Overall, the evidence suggests that topical anesthetic agents, including lidocaine spray, prilocaine/lidocaine spray, and benzocaine wipes, are effective in treating PE. These agents consistently improve IELT and patient satisfaction, with a favorable safety profile. Topical lidocaine, in particular, appears to offer substantial benefits when compared to oral medications like dapoxetine.\textsuperscript{20}

The findings also highlight the importance of individualized treatment approaches, considering patient preferences, sexual habits, and the specific characteristics of PE. Future research should focus on optimizing dosing regimens and exploring combination therapies to further enhance treatment outcomes. Additionally, long-term studies are needed to assess the sustainability of these benefits and the impact on overall sexual health and quality of life.\textsuperscript{21}
CONCLUSION

Overall, the evidence suggests that topical anesthetic agents are effective in treating PE. These agents consistently improve IELT and patient satisfaction, with a favorable safety profile. The findings also highlight the importance of individualized treatment approaches, considering patient preferences, sexual habits, and the specific characteristics of PE.

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