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Hyoscine Butylbromide, Lidocaine-Prilocaine Spray, and Placebo for Hysterosalpingography Pain: A Randomised Trial

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ABSTRACT

Background & Objective: Hysterosalpingography (HSG) is commonly associated with moderate-to-severe pain arising from both cervical instrumentation and uterine distension. We compared the efficacy and safety of oral hyoscine butylbromide, topical Lidocaine-Prilocaine (LP) spray, and a placebo for pain relief during hysterosalpingography in women with primary infertility.

Materials & Methods: In this randomized controlled trial, 102 women with primary infertility were randomized in a 1:1:1 ratio to receive oral hyoscine butylbromide (20 mg) with a placebo spray, topical lidocaine-prilocaine spray with a placebo tablet, or a double placebo. Pain was self-rated on an 11-point numerical rating scale at predefined procedural time points. The primary outcome was pain intensity during cervical instrumentation.

Results: Pain scores during cervical instrumentation differed significantly among the groups (P<0.001), being lowest in the topical lidocaine–prilocaine spray group (3.5±1.3) and highest in the placebo group (7.5±1.6). Pain during uterine filling also differed significantly between the groups (P<0.001); both active interventions reduced pain compared with the placebo, with the lowest score observed in the hyoscine group (3.7±1.5). Patient satisfaction was higher in both active intervention arms (P<0.001), and rescue analgesia was required less frequently. No serious adverse events occurred in any of the study groups.

Conclusion: Compared with the placebo, both oral hyoscine butylbromide and topical lidocaine-prilocaine spray effectively reduced pain associated with hysterosalpingography. Topical lidocaine-prilocaine spray demonstrated the greatest reduction in pain during cervical instrumentation, while both active interventions reduced pain during uterine filling. Additionally, both interventions improved patient satisfaction, reduced the need for rescue analgesia, and were well tolerated.

Keywords: Hyoscine butylbromide, Hysterosalpingography, Lidocaine-prilocaine, Primary infertility, Procedural pain, Randomised controlled trial

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1. Introduction

Infertility affects about 17.5% of adults worldwide during their reproductive life, with minimal variation across high-, middle-, and low-income countries **(1)**. Assessing tubal patency and the uterine cavity is central to the infertility work-up, as tubal factors account for a substantial share of cases **(2,3)**. Hysterosalpingography (HSG) remains a widely used first-line test because it is accessible, minimally invasive, cost-effective, and reproducible for detecting tubal obstruction **(4,5)**, including hydrosalpinx, the detection of which can alter management before assisted reproduction **(6)**. It also depicts the uterine cavity contour and can reveal Müllerian anomalies **(7)**. Consequently, it is among the initial investigations

performed in couples undergoing fertility assessment (8).

HSG is considered one of the more uncomfortable office gynaecological procedures, and pain is the most common complaint, reported as moderate-to-severe by a substantial proportion of women (9). This discomfort increases pre-procedural anxiety, may compel the operator to abandon the study before obtaining adequate imaging, and can deter women from returning for further investigation (10). The pain arises from two distinct sources: grasping the cervix with a tenaculum and passing the cannula through the internal os produce somatic cervical pain, whereas uterine distension and reflex smooth-muscle spasm resulting from contrast injection generate a deeper, cramping visceral pain (11).

Because of these distinct mechanisms, no single analgesic has proven uniformly effective. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), paracervical blocks, intrauterine lidocaine, topical cervical anaesthetics, and antispasmodics have all been evaluated with inconsistent results (12-16). More recently, a randomized double-blind trial found that pre-emptive intravenous ibuprofen reduced procedural pain and improved patient satisfaction during HSG, reflecting the continued interest in identifying effective analgesic strategies for this procedure (17). A Cochrane review found no consensus on the most effective method (18), and a subsequent network meta-analysis similarly judged the evidence limited and heterogeneous, with many trials hampered by small sample sizes and differing outcome definitions (19).

Two pharmacologically distinct agents are of particular interest, each targeting a different component of procedural pain. Topical local anaesthetics, including lidocaine-prilocaine and lidocaine sprays, act on cervical mucosal nociceptors and reduce pain most effectively during instrumentation, though with less consistent benefit in later phases (11,20,21). Hyoscine butylbromide is an antispasmodic that relieves smooth-muscle spasm, and a systematic review indicated that it reduces pain during and after the procedure (22). Although individual trials vary, recent pooled and trial evidence supports its benefit during HSG (22-26).

Together, these agents target complementary pathways -- one peripheral and cervical, the other visceral and spasmodic -- making a direct comparison clinically meaningful. To our knowledge, no randomised trial has compared oral hyoscine butylbromide, topical lidocaine prilocaine spray, and a placebo using a double-dummy design to preserve blinding across both oral and topical routes. We therefore compared their efficacy and safety for pain reduction during HSG. The primary outcome was pain during cervical instrumentation, with pain during uterine filling as a prespecified key secondary outcome. We hypothesized that topical anesthesia would primarily reduce instrumentation pain, while hyoscine would reduce the cramping pain associated with uterine filling.

2. Materials and Methods

Study Design and Setting

This single-centre, three-arm, randomised, double-blind, double-dummy, placebo-controlled trial was conducted at the Department of Obstetrics and Gynaecology, Algezeera Hospital, Giza, Egypt, and is reported in accordance with the CONSORT 2010 guidelines (27). Recruitment occurred from October 2025 to April 2026. The protocol was approved by the Algezeera Hospital Ethics Committee (EC-AJH-2025-0068) and prospectively registered at ClinicalTrials.gov (NCT07383571) prior to the enrolment of the first participant. Protocol amendments made during the planning stage were reviewed and approved by the Ethics Committee prior to the commencement of recruitment and randomisation. The registry entry was subsequently updated to reflect the final, ethics-approved protocol, including the study design, interventions, predefined outcomes, and assessment time points. The study adhered to the principles of the Declaration of Helsinki (28), and written informed consent was obtained from all participants prior to any study-related procedures.

Participants

Women aged 18–40 years with primary infertility who were scheduled for HSG as part of their routine work-up were assessed for eligibility. Inclusion criteria required participants to have regular menstrual cycles, be scheduled during the early proliferative phase (days 6-12), and have a negative urine pregnancy test on the day of the procedure.

Women were excluded if they had secondary infertility; known hypersensitivity to hyoscine, lidocaine or prilocaine; used any systemic analgesic, sedative, or antispasmodic medication within 24 hours prior to the HSG; suffered from chronic pelvic pain or severe dysmenorrhoea requiring regular analgesia; or had an active pelvic infection, known uterine anomaly, cervical stenosis requiring anaesthesia, contrast allergy, inability to cooperate with pain scoring, current pregnancy, or severe systemic disease (American Society of Anesthesiologists [ASA] physical status class III or higher).

Sample Size Calculation

Sample size calculation was based on the primary outcome of pain intensity during cervical instrumentation. Previous trials regarding hysterosalpingography analgesia (11,23) reported pain-score standard deviations ranging from 1.8 to 2.2 points on a 0-10 (11-point) numerical rating scale; a between-group difference of 1.5 points was considered clinically meaningful. Using G*Power (version 3.1) for a one-way analysis of variance (ANOVA) across three groups (two-sided α=0.05, power=80%), a minimum

of 32 participants per group was required. To account for potential missing data and protocol deviations, this was increased to 34 participants per group, resulting in a total sample size of 102.

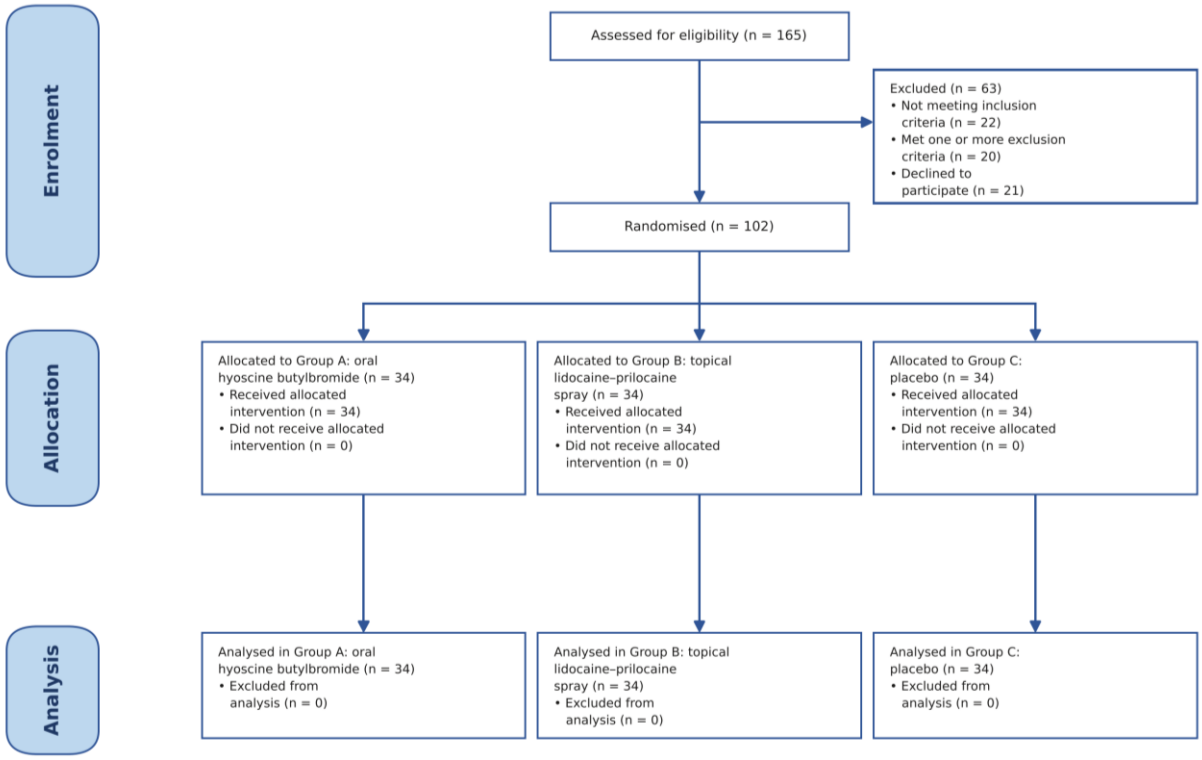


Figure 1. CONSORT flow diagram showing enrolment, randomisation, allocation, and analysis of women undergoing hysterosalpingography in the oral hyoscine butylbromide, topical lidocaine-prilocaine spray, and placebo groups.

Randomization, Allocation Concealment, and Blinding

Participants were randomly assigned 1:1:1 to the three groups using a computer-generated sequence in permuted blocks, created by an independent statistician not involved in participant recruitment, intervention, outcome assessment, or data analysis. Allocation was concealed in sequentially numbered, opaque, sealed, tamper-evident envelopes, which were opened only after enrolment by an independent pharmacist who prepared the study medications.

A double-dummy design was used to maintain blinding: each participant received one oral tablet and one cervical preparation, with the active treatment in each arm paired with a matching placebo administered by the alternative route. Placebo tablets were matched to the hyoscine tablets in size, shape, and color, and the placebo cervical preparation consisted of sterile normal saline in identical containers. Participants, the radiologist, the clinician administering the medication, the outcome assessor, and the statistician were all blinded to treatment allocation. The randomization code was broken only after data collection and database entry were completed.

Interventions

Participants were assigned to one of three groups

Group A (oral hyoscine): A single 20 mg oral tablet of hyoscine butylbromide was administered 30 minutes prior to HSG, combined with a placebo (saline) cervical spray applied 10 minutes before the procedure.

Group B (topical lidocaine-prilocaine spray): Topical lidocaine-prilocaine spray (Manovipercaine Plus, EVA Pharma, Egypt; 15% lidocaine and 5% prilocaine) was administered as three sprays to the ectocervix and external cervical os 10 minutes before HSG, combined with a placebo oral tablet administered 30 minutes before the procedure.

Group C (double placebo): A placebo oral tablet was administered 30 minutes before HSG, along with a placebo cervical spray 10 minutes before the procedure, following the same timing as the active arms.

The timing of administration was based on pharmacological profiles: oral hyoscine butylbromide reaches efficacy within approximately 30 minutes, whereas mucosal lidocaine-prilocaine becomes

effective within 5-10 minutes. Prophylactic NSAIDs, opioids, sedatives, or additional antispasmodics were strictly prohibited before or during the procedure. Antibiotic prophylaxis was administered uniformly across all groups in accordance with local clinical guidelines.

HSG Procedure

All HSG procedures were performed during the early proliferative phase (days 6-12) by a single experienced radiologist using a standardized technique. After bladder emptying and placement in the dorsal lithotomy position, a bivalve (Cusco) speculum was introduced, and the cervix and vagina were cleaned with povidone-iodine. The anterior cervical lip was grasped with a single-tooth tenaculum, with coughing encouraged when feasible to reduce discomfort. A standard metal cannula was then introduced through the external os. Water-soluble iodinated contrast was injected slowly under intermittent fluoroscopy; spot radiographs were obtained to visualize the uterine cavity, both fallopian tubes, and free peritoneal spill, with a delayed film performed when required. No additional analgesia or sedation was administered during the procedure. The radiologist and nursing staff adhered to a standardized protocol for HSG performance and pain assessment. Data were entered into an electronic case report form, and any protocol deviations or concomitant medications documented prospectively.

Outcome Measures

Pain was self-rated on an 11-point numerical rating scale (0=no pain, 10=worst imaginable) **(29)**. The primary outcome was pain during cervical instrumentation, recorded within one minute of tenaculum placement and cannulation.

Secondary outcomes included pain at the end of uterine filling (during or immediately after contrast injection), pain upon speculum insertion, pain 30 minutes after the procedure, and patient satisfaction at 30 minutes (0-10 scale, where 0=none and 10=maximum). Adverse effects related to the medications or the procedure were recorded during the HSG and throughout the post-procedure observation period; these included dry mouth, nausea, dizziness, blurred vision, tachycardia, vasovagal reactions, and allergic symptoms. Rescue analgesia (oral paracetamol 1,000 mg) was offered after the 30-minute assessment upon participant request, and its administration was recorded as a secondary outcome.

Statistical Analysis

Data were analysed using SPSS version 26. Continuous variables are expressed as mean±standard deviation, and categorical variables as frequencies and percentages. Given the equal group sizes (n=34 per arm), the sampling distribution of the mean was assumed to be approximately normal in accordance with the central limit theorem; therefore, one-way ANOVA was considered appropriate and robust to moderate deviations from normality. Homogeneity of variance was assessed using Levene's test; when this assumption was violated, Welch's ANOVA was applied. Significant overall ANOVA results were followed by pairwise comparisons using Tukey's post hoc test, with between-group mean differences reported as effect estimates alongside 95% Confidence Intervals (CIs). Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate, and significant overall comparisons were followed by pairwise Fisher's exact tests with Bonferroni correction. All analyses were performed on an intention-to-treat basis, and a two-sided P value of <0.05 was considered statistically significant.

3. Results

Of 165 women screened, 63 were excluded: 22 did not meet inclusion criteria, 20 met one or more exclusion criteria, and 21 declined to participate. The remaining 102 were randomised equally into the three study arms (34 per group). No participants were lost to follow-up after randomisation, and all were included in the intention-to-treat analysis. Baseline characteristics were balanced across groups regarding age, body mass index, education, residence, duration of primary infertility, and history of dysmenorrhea, previous pelvic surgery, previous pelvic infection, and previous HSG; no variable differed significantly between groups (all $P>0.05$) (Table 1).

Procedure duration ($P=0.43$) and pain scores after speculum insertion (before instrumentation; $P=0.53$) did not differ significantly among the study groups. However, pain scores differed significantly during cervical instrumentation and uterine filling (Table 2): pain during cervical instrumentation ($P<0.001$) was lowest in the topical lidocaine-prilocaine spray group and highest in the placebo group, whereas pain during uterine filling ($P<0.001$) was lowest in the hyoscine group. By 30 minutes post-procedure, residual pain was low in all study arms, with no significant differences observed ($P=0.35$). Patient satisfaction at 30 minutes differed significantly ($P<0.001$), being higher in the topical spray (8.2±1.2) and hyoscine (7.7±1.4) groups compared with the placebo group (5.9±1.5).

In Tukey's post hoc analyses, pain during cervical instrumentation was significantly lower with the topical lidocaine–prilocaine spray than with the placebo (mean difference -3.97, 95%CI= -4.81 to -3.13; $P<0.001$) and the hyoscine group (-1.65, 95%CI= -2.48 to -0.81; $P<0.001$); hyoscine also reduced pain compared with the placebo (-2.32, 95%CI= -3.16 to -1.49; $P<0.001$). During uterine filling, both active interventions reduced pain compared with the placebo (hyoscine -2.59, 95%CI= -3.47 to -1.70; topical -1.82, 95%CI= -2.71 to -0.94; both $P<0.001$); the difference between the hyoscine and topical groups was not significant (-0.76, 95% CI -1.65 to 0.12; $P=0.104$).

Patient satisfaction was higher in the topical spray (2.32, 95%CI= 1.52 to 3.12; P<0.001) and hyoscine (1.85, 95%CI= 1.05 to 2.65; P<0.001) groups compared with the placebo group, with no significant difference between the two active intervention arms (0.47, 95%CI= -0.33 to 1.27; P=0.345).

Table 1. Baseline demographic and clinical characteristics of the study groups

Variable	Group A: Hyoscine (n=34)	Group B: Topical lidocaine-prilocaine spray (n=34)	Group C: Placebo (n=34)	P-value
Age, years	27.1±3.9	28.0±3.6	26.7±3.6	0.390
BMI, kg/m²	25.8±3.4	27.3±4.1	26.1±3.5	0.225
Education level, n(%)				0.981
Secondary or below	6(17.6%)	5(14.7%)	7(20.6%)	
University	24(70.6%)	25(73.5%)	23(67.6%)	
Postgraduate	4(11.8%)	4(11.8%)	4(11.8%)	
Residence, n(%)				0.100
Urban	24(70.6%)	31(91.2%)	27(79.4%)	
Rural	10(29.4%)	3(8.8%)	7(20.6%)	
Duration of primary infertility, n(%)				0.742
< 2 years	8(23.5%)	7(20.6%)	10(29.4%)	
2-5 years	20(58.8%)	18(52.9%)	19(55.9%)	
>5 years	6(17.6%)	9(26.5%)	5(14.7%)	
History of dysmenorrhoea, n (%)	14(41.2%)	16(47.1%)	13(38.2%)	0.754
Previous pelvic surgery, n(%)	2(5.9%)	5(14.7%)	3(8.8%)	0.460
Previous pelvic infection, n(%)	5(14.7%)	4(11.8%)	6(17.6%)	0.800
Previous HSG, n(%)	3(8.8%)	7(20.6%)	4(11.8%)	0.340

Data are presented as mean ± standard deviation or n (%). The P value for duration of primary infertility represents the overall comparison across the three duration categories. BMI, body mass index; HSG, hysterosalpingography.

Table 2. Procedural duration and patient-reported outcomes according to study group

Outcome	Group A: Hyoscine (n=34)	Group B: Topical lidocaine-prilocaine spray (n=34)	Group C: Placebo (n=34)	P-value
Procedure duration, minutes	8.3±1.5	8.0±1.4	8.5±1.7	0.43
Pain after speculum insertion (pre-instrumentation), NRS 0-10	3.2±1.5	3.0±1.4	3.4±1.6	0.53
Pain during cervical instrumentation, NRS 0-10	5.2±1.4	3.5±1.3	7.5±1.6	<0.001
Pain during uterine filling, NRS 0-10	3.7±1.5	4.5±1.4	6.4±1.6	<0.001
Pain 30 minutes after HSG, NRS 0-10	2.0±1.2	1.9±1.1	2.3±1.3	0.35
Patient satisfaction at 30 min, 0-10 scale	7.7±1.4	8.2±1.2	5.9±1.5	<0.001

Data are presented as mean±standard deviation. NRS, Numerical Rating Scale (0-10); HSG, Hysterosalpingography.

Most adverse events were infrequent and did not differ significantly between groups, including nausea, dizziness, blurred vision, tachycardia, and vasovagal reactions; no allergic or serious adverse events were recorded (Table 3). Dry mouth occurred only in the hyoscine group (5/34, 14.7%; P=0.010), whereas local irritation or burning occurred only in the topical anesthetic group (4/34, 11.8%; P=0.033). The requirement for post-procedure rescue analgesia was significantly lower in the active intervention arms compared with the placebo group (hyoscine: 2.9%, topical anesthetic: 0%, placebo: 32.4%; P<0.001). Pairwise analysis (Fisher's exact test with Bonferroni correction) indicated that rescue analgesia was required significantly less frequently in the hyoscine group (2.9% vs 32.4%; adjusted P=0.008) and the topical spray group (0.0% vs 32.4%; adjusted P=0.001) compared with the placebo group; no statistically significant difference was observed between the active intervention arms (adjusted P=1.000). However, the differences in the incidence of dry mouth and local irritation between groups did not remain statistically significant following Bonferroni correction.

Table 3. Adverse effects and post-procedure rescue analgesia among the study groups

Adverse effect / safety outcome	Group A: Hyoscine (n=34)	Group B: Topical lidocaine-prilocaine spray (n=34)	Group C: Placebo (n=34)	P-value
Dry mouth, n(%)	5(14.7%)	0(0.0%)	0(0.0%)	0.010
Nausea, n(%)	2(5.9%)	2(5.9%)	1(2.9%)	1.000
Dizziness, n(%)	2(5.9%)	1(2.9%)	3(8.8%)	0.869
Blurred vision, n(%)	1(2.9%)	0(0.0%)	0(0.0%)	1.000
Tachycardia, n(%)	1(2.9%)	0(0.0%)	0(0.0%)	1.000
Vasovagal reaction, n(%)	2(5.9%)	1(2.9%)	3(8.8%)	0.869
Allergic reaction, n(%)	0(0.0%)	0(0.0%)	0(0.0%)	—
Local irritation or burning, n(%)	0(0.0%)	4(11.8%)	0(0.0%)	0.033
Post-procedure rescue analgesia, n(%)	1(2.9%)	0(0.0%)	11(32.4%)	< 0.001
Serious adverse events, n(%)	0(0.0%)	0(0.0%)	0(0.0%)	—

Data are presented as n (%). P-values were calculated using the chi-square test or Fisher's exact test, as appropriate. No P-value was calculated for outcomes with no events in any group.

4. Discussion

In this three-arm, double-blind, double-dummy, placebo-controlled trial, both active interventions reduced Hysterosalpingography (HSG)-related pain compared with the placebo; however, their efficacy varied according to the procedural phase. The topical lidocaine–prilocaine spray resulted in the lowest pain scores during cervical instrumentation (the predefined primary outcome), significantly outperforming both the placebo and hyoscine groups in post hoc analyses. During uterine filling, a key secondary outcome, both interventions reduced pain compared with the placebo, with the hyoscine group exhibiting the lowest numerical scores, although the difference between the hyoscine and topical groups did not reach statistical significance. Both interventions improved patient satisfaction and reduced the requirement for rescue analgesia, while neither affected pre-instrumentation pain, pain at 30 minutes, or procedure duration. This phase-specific pattern corresponds to the dual origin of HSG-related pain, suggesting that each agent is optimal for the specific component it is pharmacologically suited to target.

This separation maps onto the mechanisms outlined earlier: cervical grasping and cannulation generate somatic pain mediated by mucosal nociceptors, which a topical anesthetic can blunt, whereas uterine distension and reflex smooth-muscle spasm from contrast injection generate deeper, cramping visceral pain that an antimuscarinic antispasmodic is better suited to attenuate **(11)**. The finding that the topical Lidocaine-Prilocaine (LP) spray resulted in the lowest scores during instrumentation, whereas hyoscine resulted in the lowest scores during uterine filling, is consistent with the complementary-pathways rationale upon which this trial was designed.

The topical anesthetic's performance is consistent with existing evidence. Liberty et al., **(11)** found that cervical lidocaine-prilocaine reduced pain during tenaculum and cannula placement but had little effect on the deeper pain associated with contrast injection, and Karasahin et al., **(20)** similarly reported that a

lidocaine spray lowered overall HSG-related pain. A later meta-analysis confirmed that the most evident benefit of EMLA is during the instrumentation phase of HSG **(21)**, and trials comparing topical anesthesia with systemic agents report similar advantages during this phase **(30,31)**. Our results replicate these findings within a single trial: the topical arm achieved the lowest pain scores at instrumentation yet held no advantage over hyoscine during uterine filling. That a similar instrumentation-phase benefit appears with both a spray (observed here and in Karasahin et al.,) and a cream (Liberty et al.,), suggests that the effect reflects mucosal cervical anesthesia rather than the vehicle, acting on the somatic rather than the visceral component of the pain.

Our hyoscine findings differ from those of Abbas et al., **(23)**, who reported no significant analgesic benefit from oral hyoscine butylbromide during HSG. Our data may explain, rather than contradict, that result. The most plausible explanation is measurement resolution: a single peak or global score may dilute a benefit confined to a specific phase of the procedure. By scoring cervical instrumentation and uterine filling separately, our design successfully isolated the visceral, spasmodic phase during which an antispasmodic is expected to act. During uterine filling, hyoscine resulted in the lowest numerical pain score and significantly reduced pain compared with the placebo, although its advantage over the topical spray was numerical rather than statistically significant in post hoc comparisons. Differences in administration timing relative to the cramping phase, as well as the chosen pain endpoints, may also contribute to these results. Interpreted in this context, the apparent inconsistency may reflect not whether hyoscine is efficacious, but rather the specific procedural phase during which its effect is evaluated. In contrast, Oriji et al., **(26)** conducted a four-centre randomised controlled trial involving 520 women and observed that intramuscular hyoscine was associated with significantly lower pain scores during and after HSG compared with placebo. This discrepancy suggests that the route and timing of drug administration, alongside variations in outcome assessment, are likely contributors to the heterogeneity observed across studies.

These results align with the broader synthesis literature. Both the Cochrane review **(18)** and the subsequent network meta-analysis **(19)** concluded that no single method is clearly superior, attributing the uncertainty partly to small sample sizes and the wide variation in how and when pain was measured. Our findings offer a structural explanation: if pharmacological agents relieve pain in a stage-dependent manner, trials using a single pain score, or those measuring pain at a phase mismatched to the agent's mechanism, will inevitably yield conflicting or null results. A phase-specific outcome framework, such as the one employed here, may therefore provide a more robust approach for evaluating HSG analgesia in future studies.

Beyond pain scores, both active intervention arms resulted in greater patient satisfaction and a substantially lower requirement for rescue analgesia than placebo. Given that HSG-related pain can lead to the premature termination of the examination and deter women from returning for further investigations **(9)**, these patient-centred outcomes are of significant clinical importance; completing the procedure comfortably preserves the tubal-patency information necessary to guide subsequent fertility treatment, including the selection of candidates for intrauterine insemination **(32)**.

The safety profile of each intervention aligned with its known pharmacology and raised no new concerns. Dry mouth occurred only in the hyoscine group, consistent with its anticholinergic activity, whereas transient local irritation or burning occurred only in the topical anesthetic group; both effects were minor, with no allergic or serious adverse events reported in any arm. Other adverse events were infrequent and occurred at similar rates across the groups.

The primary strengths of this study include its double-dummy, double-blind design, which compared two interventions delivered via different routes against a placebo while maintaining blinding for participants, the radiologist, the outcome assessor, and the analyst. The use of a single experienced radiologist following a standardized technique, prospective trial registration, a sample size powered for the primary outcome, intention-to-treat analysis, and complete follow-up with no losses further strengthen the study's internal validity. Limitations include the relatively small sample size, the single-centre design, and the focus on a primary-infertility-only population, all of which may limit the generalizability of these findings to other centres, clinical settings, populations, including women with secondary infertility. Furthermore, the reliance on a subjective rating scale and a single operator while aiding consistency may reduce external validity. The study was also underpowered to detect significant differences between the two active interventions at each time point; therefore, the stage-specific pattern observed particularly the numerical advantage of hyoscine over the topical spray during uterine filling should be regarded as hypothesis-generating. Baseline anxiety, anticipated pain, and HSG findings, such as tubal occlusion or difficult contrast spill, were not analysed, although they may influence pain perception. Because dry mouth and local burning were arm-specific, some participants may have inferred their treatment allocation despite the double-dummy design. Finally, the absence of a combined-treatment arm prevents any conclusion regarding whether simultaneous topical anesthesia and antispasmodic therapy would provide an additive or superior effect.

5. Conclusion

Oral hyoscine butylbromide and topical lidocaine–prilocaine spray effectively reduced HSG-related pain compared with a placebo, with their efficacy varying according to the procedural stage. The topical lidocaine–prilocaine spray was most effective for pain associated with cervical instrumentation, whereas both active interventions reduced pain during uterine filling. Future studies should explore the potential benefits and risks of combining topical anesthesia with antispasmodic therapy.

6. Declarations

Acknowledgments

None.

Ethical Considerations

The study protocol was approved by the Algezeera Hospital Ethics Committee (EC-AJH-2025-0068). The study was conducted in accordance with the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants before enrolment. The trial was registered at ClinicalTrials.gov (NCT07383571). Changes made to the originally registered protocol during the study-planning stage were reviewed and approved by the Ethics Committee before participant recruitment and randomisation. The registry record was subsequently updated to reflect the final ethics-approved protocol and predefined outcomes.

Authors' Contributions

ASA conceived and designed the study. AHA, IKY, AME, SA, and MAG collected the data. MA and AA contributed to the study methodology, supervision, and interpretation of findings. MA performed the statistical analysis. ASA drafted the manuscript. MA, AHA, IKY, AA, AME, SA, and MAG critically revised the manuscript for important intellectual content. All authors reviewed and approved the final manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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