Lidocaine Spray Compared With Submucosal Injection for Reducing Pain During Loop Electrosurgical Excision Procedure

A Randomized Controlled Trial

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OBJECTIVE: To examine the effectiveness of lidocaine spray compared with conventional lidocaine submucosal injection during a loop electrosurgical excision procedure (LEEP).

METHODS: Women undergoing LEEP for any degrees of cervical intraepithelial neoplasia were invited to participate. The participants were randomly assigned into two groups. In group 1 (injection), the participants were anesthetized with 1.8 mL (36 mg) of 2% lidocaine with 1:100,000 epinephrine injected submucosally using a pressure syringe injector with a 27-gauge needle tip at 3, 6, 9, and 12 o'clock locations of the ectocervix. For group 2 (spray), the patients were locally anesthetized with four puffs (40 mg) of 10% lidocaine spray applied thoroughly to the ectocervix. The patients rated their pain according to a 10-cm visual analog scale at different points during the procedure including baseline, postanesthesia, excision, and 30 minutes postexcision. Primary outcomes were the excision pain score and its difference from the baseline.

RESULTS: One hundred one patients (51 in the injection group and 50 in the spray group) participated in the study. The baseline pain scores, the excision pain scores, the difference between the excision and the baseline pain scores, and the postexcision pain scores were comparable between the study groups. The median postanesthesia pain score and the median difference of the postanesthesia score from baseline were significantly higher in the injection group, 3.4 compared with 0.6 and 1.9 compared with 0.0, respectively ($P<.01$).

CONCLUSION: Lidocaine spray is an effective and practical alternative measure for reducing pain associated with electrical excision of the cervix during LEEP.

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LEVEL OF EVIDENCE: I

The loop electrosurgical excision procedure (LEEP) is a widely accepted minor surgical procedure for diagnosis and treatment of cervical intraepithelial neoplasia.[1,2] During the procedure, several methods of anesthetic blocks have been proposed to reduce pain.[3] Generally, intracervical submucosal injection of lidocaine is used.[4] However, from the authors' experience, there is significant pain and discomfort associated with the injection itself. Lidocaine spray is an effective measure for pain control during minor gastrointestinal and otolaryngologic procedures.[5–7] It is simple and without pain related to application. Data on the effectiveness of lidocaine spray for pain control during LEEP are lacking.

The objective of this study is to examine the effectiveness of lidocaine spray compared with conventional lidocaine submucosal injection by comparing pain scores at various stages of LEEP.

MATERIALS AND METHODS

Between October 2011 and December 2012, women undergoing LEEP at our institution for any degrees of cervical intraepithelial neoplasia detected from cervical cytology, histology, or both were invited to participate in this randomized controlled trial comparing two anesthetic techniques, lidocaine spray and lidocaine submucosal injection. Exclusion criteria

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included known history of hypersensitivity to local anesthetics of the amide type or to other components of the solution, pregnancy, heart disease using a pacemaker or cardiac arrhythmia, history of neurologic deficit, drug abuse, and local infection (cervical or vaginal infection). Informed consent was obtained from each participant enrolled. The Faculty of Medicine Research Ethics Committee approved this study.

After enrollment, demographic and clinical data were collected including age, parity, cervical cytology results at presentation, cervical punch biopsy at colposcopy, previous history of LEEP, loop diameter, cone volume, additional tophat excision, and final histology. For all cases, LEEP was performed in the outpatient setting by gynecologic oncology fellows using the uniform conventional technique. In each case, the patient was placed in the lithotomy position and the operative area was cleaned and draped. The cervix was then inspected using a sterile bivalve speculum. The operator determined a proper loop size (from the diameter of 1, 1.5, 2, 2.5, to 3 cm) to be used based on the size and contour of the cervix and the extent of the cervical lesion identified at colposcopy. At this point, the participants were randomly assigned into two groups according to a computer-generated random allocation sequence. Sequentially numbered, sealed opaque envelopes were used to provide allocation concealment. Randomization was stratified according to the loop diameter with a cutoff point of 2 cm. In group 1 (injection), the participants were anesthetized with 1.8 mL (36 mg) of Medicaine injection 2% 1:100,000 (2% lidocaine with 1:100,000 epinephrine) injected submucosally using a standard pressure syringe injector with a 27-gauge needle tip at 3, 6, 9, and 12 o'clock locations of the ectocervix. For group 2 (spray), the patients were locally anesthetized with four puffs (40 mg, 10 mg per puff) of 10% Xylocaine spray (10% lidocaine spray) applied thoroughly to the ectocervix. The participants were not told about the assigned allocation. The 3-minute waiting time was used in all participants for the anesthetics to take effect before proceeding with the procedure. Then LEEP was performed using blended cutting and coagulating mode. The additional tophat excision was performed in patients who were found to have a lesion located deep in the cervical canal. After the excision, hemostasis was generally achieved by electrocoagulation through the ball-head electrode along with local application of a hemostatic agent. After the procedure, the patients were observed for 30 minutes for any evidence of complications before being discharged home.

In each case, a research assistant asked the patient to rate her pain according to a standard 10-cm visual analog scale at different points during the procedure. These included pain scores at the beginning of the procedure immediately after speculum insertion (baseline pain score), immediately after administering anesthetic agents (postanesthesia pain score), immediately after accomplishing cone excision before proceeding with the remaining steps of the entire procedure (excision pain score), and at 30 minutes after the excision (postexcision pain score). The visual analog scale consisted of a 10-cm line scaled from 0 (no pain) to 10 (worst possible pain). Primary outcomes of this study were the excision pain score and its difference from the baseline pain score.

Sample size calculation for the study was based on the primary outcome of the difference between excision and baseline pain score. A 1-cm difference in visual analog scale between the study groups was selected as the smallest effect that would be of clinical importance. Referring to standard deviations of each study group from our pilot study with the α value set at 0.05 (two-tailed) and the power set at 80%, the sample size was calculated to be 46 patients for each group.

Statistical analysis was performed with SPSS for Windows 12. Comparison of continuous variables was made by using the two-tailed Student's *t* test. For continuous variables with skewed distribution, the Mann-Whitney *U* test was performed to compare the outcomes between the groups. The χ^2 or Fisher's exact test, as considered appropriate, was used for comparison of categorical variables. $P<.05$ was considered statistically significant. Subgroup analysis based on the loop size with the cutoff point of 2 cm was planned before the study started.

RESULTS

One hundred one patients (51 in injection group and 50 in spray group) participated in the study with no dropouts (Fig. 1). Patients in the two study groups were similar with respect to age and parity. Median age was 47 years (range 28–69 years) in the injection group and 48 years (range 28–85 years) in the spray group. Median parity was two (range 0–5) in both groups.

High-grade squamous intraepithelial lesion was the most common abnormal cervical cytology finding at presentation in both groups. The proportion of patients who had punch biopsy done at the time of colposcopy was significantly higher in the injection group, 37.3% compared with 16.0% ($P=.02$). One patient in each group had undergone prior LEEP. Loop diameter, cone volume, additional tophat excision, and final histology were comparable between the groups (Table 1).

Table 2 compares pain scores at various stages of the procedure between the injection and the spray groups. The baseline pain scores, the excision pain scores, the difference between the excision and the

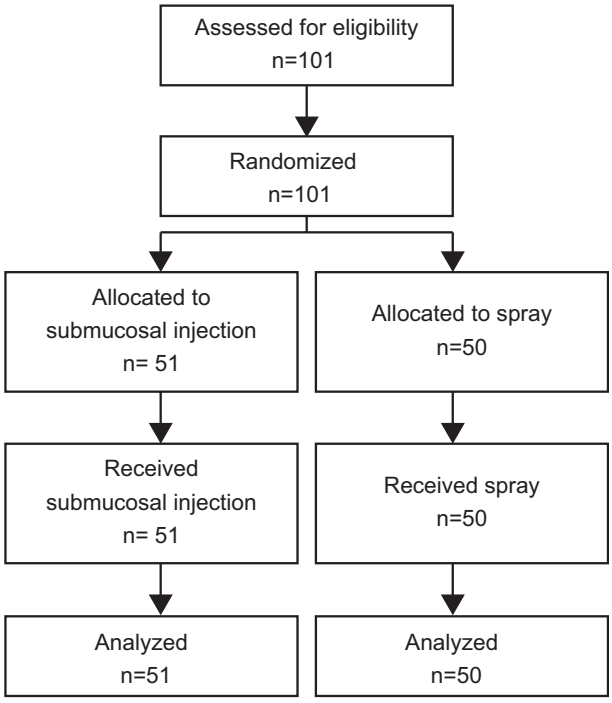

Fig. 1. Flow of participants through the study.

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baseline pain scores, and the postexcision pain scores were comparable between the study groups. The median postanesthesia pain score and the median difference of the postanesthesia score from baseline were significantly higher in the injection group, 3.4 compared with 0.6 and 1.9 compared with 0.0, respectively ($P<.01$). The subgroup analysis with regard to loop diameter demonstrated similar findings. For the injection group, the mean postanesthesia pain scores were 3.1 in the patients with previous punch biopsy during colposcopy compared with 4.3 in those without previous biopsy ($P=.11$). Median satisfaction scores were comparable between the study groups, 8.5 (range 0.8–10.0) in the injection group and 8.5 (range 5.0–10.0) in the spray group ($P=.83$). There was no complication observed in any participants.

DISCUSSION

Similar to other minor procedures performed on the cervix such as laser ablation or cryosurgery, some forms of local anesthesia are needed to reduce pain associated with LEEP. Our data demonstrating a significant pain level associated with the electrical excision of the cervix, a visual analog scale score of 4 in the injection group and 3 in the spray group even with the use of local anesthesia, have confirmed this need. Generally, submucosal or paracervical block is used during these procedures.[3,8–10] However, from our experience, the anesthetic injection itself is associated with significant pain and discomfort. Anesthetic spray, as used in minor gastrointestinal and otolaryngologic procedures, would potentially solve this problem.

The data from this study have suggested that lidocaine spray and lidocaine submucosal injection are equally effective in reducing pain associated with electrical loop excision of the cervix. In addition, the application of the lidocaine spray is associated with significantly less pain. This is the case regardless of the loop diameter used. Data on a minimal clinically significant difference in pain as measured by the visual analog scale pain scores for the patients undergoing LEEP are lacking. However, published articles in the field of emergency medicine have shown that the minimal clinically significant differences for acute pain in the setting of emergency department were 9 and 12 mm, respectively. According to these studies, there was no significant difference in minimal clinically significant difference from visual analog scale pain

Table 1. Clinical, Pathologic, and Operative Characteristics

Characteristic	Injection (n=51)	Spray (n=50)	*P*
Cervical cytology results			.19
No epithelial lesion	2 (3.9)	0 (0.0)	
ASC-US	3 (5.9)	5 (10.0)	
LSIL	12 (23.5)	9 (18.0)	
ASC-H	8 (15.7)	6 (12.0)	
HSIL	20 (39.2)	29 (58.0)	
Squamous cell carcinoma	4 (7.8)	1 (2.0)	
Adenocarcinoma	2 (3.9)	0 (0.0)	
Final histology			.79
No epithelial lesion or cervicitis	14 (27.5)	14 (28.0)	
LSIL	8 (15.7)	7 (14.0)	
HSIL or AIS	22 (43.1)	25 (50.0)	
Carcinoma	7 (13.7)	4 (8.0)	
Cervical biopsy at colposcopy	19 (37.3)	8 (16.0)	.02
Loop diameter (cm)			.91
1.0	1 (2.0)	0 (0.0)	
1.5	14 (27.5)	14 (28.0)	
2.0	24 (47.1)	24 (48.0)	
2.5	8 (15.7)	8 (16.0)	
3.0	4 (7.8)	4 (8.0)	
Cone volume (cm^3)	2.5 (0.2–13.5)	2.7 (0.9–8.3)	.52
Tophat	26 (51.0)	18 (36.0)	.13

ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesions; ASC-H, atypical squamous cells, cannot exclude HSIL; HSIL, high-grade squamous intraepithelial lesions; AIS, adenocarcinoma in situ.

Data are n (%) or median (range) unless otherwise specified.

Table 2. Pain Scores

Characteristic	Injection	Spray	*P*
Overall (N=101)			
Baseline	1.4 (0.0–7.2)	1.2 (0.0–9.3)	.53
Postanesthesia	3.4 (0.0–8.6)	0.6 (0.0–8.7)	<.01
Postanesthesia to baseline difference	1.9 (−3.5 to 7.6)	0.0 (−5.7 to 3.0)	<.01
Excision	4.0 (0.0–8.2)	3.0 (0.0–9.5)	.11
Excision to baseline difference	2.1 (−3.9 to 6.1)	1.5 (−5.4 to 7.7)	.13
Postexcision	1.9 (0.0–8.5)	2.6 (0.0–7.8)	.84
Loop diameter 2 cm or more (n=71)			
Baseline	1.3 (0.0–6.2)	1.2 (0.0–9.3)	.57
Postanesthesia	3.6 (0.0–8.6)	0.5 (0.0–8.7)	<.01
Postanesthesia to baseline difference	1.9 (−2.8 to 7.6)	0.0 (−5.0 to 3.0)	<.01
Excision	4.3±2.3	3.8±2.7	.41
Excision to baseline difference	2.3±2.1	1.9±2.6	.53
Postexcision	1.8 (0.0–8.5)	3.0 (0.0–7.8)	.45
Loop diameter less than 2 cm (n=30)			
Baseline	1.5 (0.0–7.2)	0.8 (0.0–6.5)	.82
Postanesthesia	3.3 (0.3–8.5)	1.0 (0.0–6.4)	<.01
Postanesthesia to baseline difference	1.8 (−3.5 to 4.9)	0.0 (−5.7 to 1.7)	<.01
Excision	3.4 (0.0–7.9)	1.4 (0.0–7.8)	.10
Excision to baseline difference	1.7 (−1.4 to 6.1)	0.4 (−5.4 to 3.3)	.17
Postexcision	2.0 (0.3–6.4)	0.9 (0.0–7.6)	.33

Data are median (range) or mean±standard deviation unless otherwise specified.

scores with regard to age, sex, cause of pain, and severity of pain.[11,12] Based on these data, the difference in pain associated with the route of anesthetic administration demonstrated in the present study would appear significant clinically. Of note, the spraying procedure is simple without the need for special instruments. Furthermore, with the use of lidocaine spray in place of injection, the risk of needlestick injury can be avoided.

The strength of this study is the prospective randomized controlled trial design with allocation concealment and a priori subgroup analysis. The procedure was performed using a uniform technique with operators of the same level. All participants provided data for final analysis of the main outcomes in the assigned study groups without dropouts.

However, certain limitations exist. First, the dosages of lidocaine used in the study groups were not exactly the same, 36 mg in the injection group and 40 mg in the spray group. For a conventional lidocaine injection during LEEP at our institution, a fixed dose of 2% lidocaine with 1:100,000 epinephrine in a 1.8-mL ampule specifically designed for use with a pressure syringe is routinely used. When applying 10% lidocaine spray with a fixed dose of 10 mg per puff in this study, it was not possible to use the exact same dosage for both groups. Therefore, we chose the 40-mg dosage for the spray group because it was closest to the routine dosage for injection. Keeping this in mind, the interpretation of the results of this study should be based on the comparison of two different approaches rather than the anesthetic dosage, which is part of the entire process. Also, this dosage difference would not affect the postanesthesia pain results, which were basically associated with the route of anesthetic administration rather than the anesthetic dosage. Second, there was an imbalance in the proportion of patients who had previous punch biopsy at colposcopy between the groups with a higher proportion in the injection group. However, when the postanesthesia pain score in the injection group was further examined, the scores for the patients with and without previous biopsy were comparable with a trend toward less pain in those who had previous biopsy. Therefore, one could assume that the effect of previous biopsy on postanesthesia pain, if any, would be in favor of the injection group. In fact, this information has strengthened our finding. Third, the blinding process was incomplete. An attempt was made to blind the participants from the assigned allocation during the procedure. However, complete blinding of the participants would not be achievable as a result of the nature of the procedure (the injection). Also, blinding of the operators would not be practical in this situation. Finally, the sample size of this study may not be adequate for the detection of a small difference in secondary outcomes such as the 30-minute postexcision pain score between the study groups.

In conclusion, lidocaine spray is an effective and practical alternative measure for reducing pain associated with electrical excision of the cervix during LEEP. Further exploration of its use in other procedures for the management of local lesions involving lower genital tract would be worthwhile.

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