Lidocaine Does Not Reduce Pain Perception during Gel Instillation Sonography or Subsequent Office Hysteroscopy: Results of a Randomized Trial

T. Van den Bosch\textsuperscript{a} D. Van Schoubroeck\textsuperscript{a} A. Daemen\textsuperscript{b} E. Domali\textsuperscript{a}
V. Vandenbroucke\textsuperscript{a} B. De Moor\textsuperscript{b} J. Deprest\textsuperscript{a} D. Timmerman\textsuperscript{a}

\textsuperscript{a}Department of Obstetrics and Gynaecology, University Hospitals Leuven, and \textsuperscript{b}Department of Electrical Engineering, ESAT-SCD, K.U. Leuven, Leuven, Belgium

Conclusion: The addition of lidocaine to the gel used either for GIS or prior to office hysteroscopy does not reduce the procedure-related pain.

Introduction

Several diagnostic modalities are currently used to explore abnormal uterine bleeding, including transvaginal ultrasound with or without contrast infusion, (office) hysteroscopy and endometrial sampling. Although those techniques are well accepted, patients may still experience moderate to severe pain during some of the procedures\textsuperscript{1}. Recently the instillation of gel instead of saline has been proposed for sonohysterography\textsuperscript{2}. In an earlier prospective observational cohort study, we observed that the procedure-related pain during contrast sonohysterography, as well as during subsequent hysteroscopy and endometrial sampling was less in the gel infusion sonohysterography (GIS) group as compared to the saline contrast sonohysterography group\textsuperscript{3}.

The aim of the present randomized study was to evaluate if the addition of lidocaine to the gel used for GIS would further reduce the pain as experienced during GIS.
Secondly, we evaluated if the addition of lidocaine to gel instilled prior to office hysteroscopy reduces the procedure-related pain. The effect of gel with and without lidocaine was compared.

**Materials and Methods**

This study was a randomized clinical trial conducted between December 2006 and October 2007 at the Department of Gynaecology of the University Hospitals Leuven, Belgium. The study was approved by the hospital’s Medical Ethics Committee, and written informed consent was provided by all patients.

A total of 142 consecutive patients presenting at the department’s One-Stop Bleeding Clinic were randomized into one of the two groups using numbers generated randomly by a computer [http://www.random.org/integers/]. The numbers were picked independently of each other and may therefore contain duplicates. Because the randomness comes from atmospheric noise, meaning that the numbers are picked independently of each other like rolls of a die, the distribution is not necessarily 50/50. The allocations were placed in opaque-sealed numbered envelopes. The ultrasound was performed using a GE Voluson E8 ultrasound machine with a 3D transvaginal probe. Gels with and without lidocaine were used. Both gels are commercially available and have an identical content (sodium lactate, chlorhexidine digluconate, methyl p-hydroxybenzoate and propyl p-hydroxybenzoate) besides that Endosgel® (Farco-Pharma GmbH, Cologne, Germany) does not contain lidocaine, while Instillagel® (Farco-Pharma GmbH) does contain 2% lidocaine. The gel was warmed to 37°C to increase viscosity and to facilitate the instillation and was infused through a 2.0-mm neonatal suction catheter. All GIS were performed by the same examiner (T.V.). GIS failed in 3 patients due to cervical stenosis. Within 30 min after GIS, 132 patients (94%) underwent office hysteroscopy according to the department’s bleeding clinic’s protocol. Hysteroscopy was performed without local anesthesia using a 3-mm rigid Storz® hysteroscope with a single inflow channel: a speculum was inserted and the cervix was cleaned with a water solution of cetrimonium bromide 0.5% and chlorhexidine 0.05%. The hysteroscopy was performed mostly without the use of a tenaculum and without dilatation of the cervix. Distention of the cavity was achieved by normal saline and the pressure for distending the cavity was supplied by a pressure cuff pumped up to 0.1 bar. The speculum was removed once the scope had been inserted through the cervical canal.

The patients as well as the medical staff performing the hysteroscopy were unaware which gel had been used. The examiner performing the GIS however was aware of the random allocation. The women were asked to fill in a questionnaire including a 100-mm visual analogue scale (VAS) score about their pain perception during the different procedures: 0 indicating the procedure was not painful at all, and 100 indicating it was the most painful experience one could imagine. The patients had time to fill it in after the ultrasound/GIS procedure and after the hysteroscopy. They completed the questionnaire without the help of any staff member, and were asked to return it at the desk before leaving the clinic.

Table 1. Patients’ characteristics

<table>
<thead>
<tr>
<th></th>
<th>GIS group</th>
<th>Hysteroscopy group</th>
<th>Gel with lidocaine</th>
<th>Gel without lidocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>142</td>
<td>132</td>
<td>79</td>
<td>63</td>
</tr>
<tr>
<td>Age, years</td>
<td>50.8 ± 12.1</td>
<td>50.6 ± 12.4</td>
<td>49.4 ± 11.4</td>
<td>52.5 ± 12.8</td>
</tr>
<tr>
<td>Menopausal status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>55 (38.7%)</td>
<td>51 (38.6%)</td>
<td>25 (31.6%)</td>
<td>30 (47.6%)</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>83 (58.5%)</td>
<td>78 (59.1%)</td>
<td>52 (65.8%)</td>
<td>31 (49.2%)</td>
</tr>
<tr>
<td>Perimenopausal</td>
<td>4 (2.8%)</td>
<td>3 (2.3%)</td>
<td>2 (0.3%)</td>
<td>2 (3.2%)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nullipara</td>
<td>22 (15.6%)</td>
<td>21 (15.9%)</td>
<td>12 (15.4%)</td>
<td>10 (15.9%)</td>
</tr>
<tr>
<td>Endometrial thickness on ultrasound, mm</td>
<td>7.9</td>
<td>7.5</td>
<td>7.9</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td>5.1–11.9</td>
<td>4.9–11.9</td>
<td>5.5–11.6</td>
<td>4.5–12</td>
</tr>
</tbody>
</table>

SD = Standard deviation; IR = interquartile range. 'Postmenopausal' status was defined as more than 12 months’ amenorrhea in non-pregnant women over age 40; 4 women in whom the menstrual history was equivocal were categorized as 'perimenopausal'.
appropriately used to determine the statistical significance of differences in the categorical variables menopausal status, parity and final diagnosis. Statistical analysis was performed using SAS Version 9.1 for Windows. Two-sided p values are reported. A probability level of 0.05 was chosen for statistical significance.

**Results**

Of the 142 randomized patients, 79 were allocated to gel with lidocaine (Instillagel), whereas 63 patients received a gel without lidocaine (Endosgel). The mean age (SD) was 50.8 (12.1) years; 58.5% were premenopausal and 15.6% were nulliparous (table 1). The results of the final diagnosis are given in table 2. Altogether 99 patients (70%) returned the questionnaire including the VAS score.

The median (interquartile range (IR) VAS score during GIS was 6 (19.5) for the total group; 8 (21) for the lidocaine group versus 5 (18.2) for those who received gel without lidocaine. The median (IR) VAS scores during hysteroscopy in the total group, the Instillagel group and the Endosgel group were 15.5 (43.2), 24 (35) and 9 (52), respectively (table 3). None of the differences were statistically significant.

No major adverse effects were observed during the study, and all patients were able to leave the clinic within 1 h after the last examination.

**Discussion**

In the present randomized trial we showed that the addition of lidocaine to the gel – used either for GIS or prior to office hysteroscopy – does not reduce procedure-related pain. In a previous study we reported lower pain scores during contrast sonography of the uterine cavity as well as during subsequent hysteroscopy and endometrium biopsy when gel was used instead of saline for contrast sonohysterography [3]. Gel may facilitate transcervical instrumentation due to its lubrication qualities, causing less discomfort for the patient. Although procedure-related pain is considered tolerable during saline contrast sonohysterography or hysteroscopy [4], some patients might benefit from some pain relief. Different stud-

---

**Table 2. Final diagnosis**

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th>GIS group</th>
<th>Hysteroscopy group</th>
<th>p value</th>
<th>Gel with lidocaine</th>
<th>Gel without lidocaine</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal findings</td>
<td>85</td>
<td>80</td>
<td></td>
<td>45</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Endometrial hyperplasia without atypia</td>
<td>4</td>
<td>4</td>
<td></td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Endometrial polyp</td>
<td>36</td>
<td>35</td>
<td></td>
<td>20</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Intracavity myoma</td>
<td>12</td>
<td>10</td>
<td></td>
<td>10</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Endometrial malignancy</td>
<td>5</td>
<td>3</td>
<td></td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>142</td>
<td>132</td>
<td>0.98</td>
<td>79</td>
<td>63</td>
<td>0.32</td>
</tr>
</tbody>
</table>

1 Including endometrial atrophy, proliferative- and secretory changes. The ‘final diagnosis’ has been based on ultrasound findings (n = 7), hysteroscopy findings (n = 14), histological examination after endometrial sampling (n = 63), histological examination after resection of a lesion at operative hysteroscopy (n = 42) or the pathological examination of the hysterectomy specimen (n = 16).

**Table 3. Pain scores during GIS and office hysteroscopy**

<table>
<thead>
<tr>
<th></th>
<th>Gel with lidocaine (n = 79)</th>
<th>Gel without lidocaine (n = 63)</th>
<th>Total (n = 142)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS-GIS Responders</td>
<td>59</td>
<td>40</td>
<td>99</td>
<td>0.5423</td>
</tr>
<tr>
<td>Median</td>
<td>8</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>IR</td>
<td>2–23</td>
<td>1–19.2</td>
<td>1.5–21</td>
<td></td>
</tr>
<tr>
<td>VAS Hyst Responders</td>
<td>57</td>
<td>37</td>
<td>94</td>
<td>0.7486</td>
</tr>
<tr>
<td>Median</td>
<td>24</td>
<td>9</td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td>IR</td>
<td>5–40</td>
<td>4–56</td>
<td>5–48.2</td>
<td></td>
</tr>
</tbody>
</table>

VAS = Visual analogue scale (mm); GIS = gel infusion sono-hysterography; Hyst = office hysteroscopy; IR = interquartile range; Responders = number of patients who responded to the questionnaire.
ies showed that anesthesia of the cervix, either by para-
cervical block [5] (randomized open label trial, using 1% mepi-
vacaine) or using topical lidocaine gel [6] (random-
ized double-blind, placebo-controlled) does not reduce
the pain experienced during hysteroscopy or endometri-
al sampling. Studies on the use of topical anesthesia into
the uterine cavity give conflicting results. Two relatively
small randomized double-blind studies using mepi-
vacaine injected through the cervix prior to hysteroscopy
or endometrial sampling found a beneficial effect [7, 8].
Using lidocaine 2% prior to endometrial biopsy, Hui et al.
[9] also reported lower pain scores in the treated group,
whereas both Lau et al. [10] (90 patients) and Wong et al.
[6] (500 women) did not find any improvement in the
pain experienced during hysteroscopy or endometrial
sampling after lidocaine instillation (all three studies [6, 9, 10] were randomized and double-blind). The only ran-
domized study using intrauterine lidocaine 2% gel [11]
prior to Vabra endometrial sampling in 308 patients did
not show any pain reduction in the lidocaine group.

The limitation of the study is the dropout rate of 30%,
caused by the number of patients who failed to return the
questionnaire. This may preclude definitive conclusions.
However, since the comparison between gel with and
without lidocaine was performed for each procedure sep-
arately, and since, at randomization, the numbers gener-
ated randomly by a computer were picked independently
of each other, our data are still relevant. However, our
conclusions should be confirmed in a larger series.

In conclusion, the present randomized trial demon-
strates no beneficial effect on patients’ pain perception
when adding lidocaine to the gel used for GIS or applied
prior to other transcervical procedures. However, defini-
tive conclusions should be confirmed by a larger series.

References

1. Van den Bosch T, Verguts J, Daemen A, Ge-
vart O, Domali E, Claerhout F, Vandenvoucke V, De Moor B, Deprest J, Timmer-
man D: Pain experienced during transvaginal ultrasound, saline contrast sonohysterogra-
phy, hysteroscopy and office sampling: a comparative study. Ultrasound Obstet Gyn-

2. Exalto N, Stappers C, van Raamsdonk L.A, Emanuel M.H: Gel instillation sonohysterog-

infusion sonography in the evaluation of the uterine cavity. Ultrasound Obstet Gynecol
2009;34:711–714.

sampling and hysteroscopic endometrial bi-
opsy: a comparative study. Ultrasound Ob-

anesthesia for outpatient hysteroscopy. Fer-

pain score analysis of the effect of local lig-
ocaine on outpatient hysterectomy: a ran-
domized, double-blind, placebo-controlled

7. Cicinelli E, Didonna T, Ambrosi G, Schönau-
er LM, Fiore G, Matteo MG: Topical anes-
thesia for diagnostic hysteroscopy and endo-
metrial biopsy in postmenopausal women:
 a randomized placebo-controlled double-
blind study. Br J Obstet Gynaecol 1997;104:
316–319.

anesthesia in diagnostic hysteroscopy and endometrial biopsy. Fertil Steril 1995;63:
414–416.

9. Hui SK, Lee L, Ong C, Yu V, Ho LC: Intra-
uterine lignocaine as an anaesthetic during
endometrial sampling: a randomized dou-
ble-blind controlled trial. BJOG 2006;113:
53–57.

10. Lau WC, Tam WH, Lo WK, Yuen PM: A ran-
domised double-blind placebo-controlled
trial of transcervical intrauterine local an-
eaesthesia in outpatient hysterectomy. BJOG

ine application of two percent lignocaine gel
on pain perception during Vabra endome-
trial sampling: a randomised double-blind,
placebo-controlled trial. BJOG 2001;108:87–
90.