Comparison of four different pain relief methods during hysterosalpingography: A randomized controlled study

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BACKGROUND: Hysterosalpingography (HSG) is the most commonly used method for evaluating the anatomy and patency of the uterine cavity and fallopian tubes, and is an important tool in the evaluation of infertility. The most frequent side effect is the pain associated with the procedure.

OBJECTIVES: To evaluate four analgesic methods to determine the most useful method for reducing discomfort associated with HSG.

METHODS: In the present prospective study, 75 patients undergoing HSG for evaluation of infertility were randomly assigned to four groups: 550 mg of a nonsteroidal anti-inflammatory drug (NSAID) (group 1); 550 mg NSAID + paracervical block (group 2); 550 mg NSAID + paracervical analgesic cream (group 3); or 550 mg NSAID + intrauterine analgesic instillation (group 4). A visual analogue scale was used to assess the pain perception at five predefined steps.

RESULTS: Instillation of the liquids used for HSG was found to be the most painful step of HSG, and this step was where the only significant difference among groups was observed. When comparing visual analogue scale scores, group 2 and group 3 reported significantly less pain than the other groups. Group 1 reported significantly higher mean (± SD) scores (7.2±1.6) compared with groups 2 and 3 (4.7±2.5 and 3.8±2.4, respectively) (P<0.001). In addition, group 2 reported significantly less pain than group 4 (4.7±2.5 versus 6.7±1.8, respectively) (P<0.02).

CONCLUSIONS: For effective pain relief during HSG, in addition to 550 mg NSAID, local application of lidocaine cream to the posterior fornix of the cervix uteri and paracervical lidocaine injection into the cervix uteri appear to be the most effective methods.

Key Words: Hysterosalpingography; Intrauterine lidocaine; Lidocaine cream; Pain relief; Paracervical block; Visual analogue scale

In developed countries, the prevalence of infertility is approximately 12% (6.6% to 26.4%) among those of reproductive age (1). Infertility is clinically defined as the failure to achieve a pregnancy after ≥12 months of regular unprotected sexual intercourse (2). The factors that affect female fertility include pathologies involving the uterus, cervix, ovaries, fallopian tubes, endometrium and peritoneum. Fallopian tube abnormalities account for 30% to 40% of all female infertility cases (3).

Hysterosalpingography (HSG) is the fluoroscopic evaluation of the female genital tract after injection of a radio-opaque medium through the cervical canal (1). It is commonly used to determine the causes of infertility and frequent miscarriages by examining the internal luminal morphology of the endocervical canal, uterine cavity and fallopian tubes, and associated abnormalities such as congenital anomalies, neoplasia and inflammatory changes (4,5). The number of HSGs performed per year has gradually increased with the increasing rate of infertility (eg, approximately 7.2% of the reproductive-age population in developed countries) (5).

HSG is performed during the proliferative phase, after cessation of menstruation and before ovulation, between days 7 and 11, to avoid any early pregnancies (6). This diagnostic test was originally performed with oil-soluble contrast media, but now most clinicians use water-soluble media for its cost and imaging advantages.

Pain is the most frequent side effect of HSG. Although the pain perception gradually decreases after the intervention and typically ends in 30 min, up to 72% to 80% of patients report mild to moderate pain during the procedure (7,8). Nevertheless, most women (59%) describe this diagnostic procedure as very stressful (9). The majority of women regard a hysterosalpingogram as acutely painful because it involves placement of a cervical tenaculum, traction on the cervix, instillation of dye through a cervical cannula and tubal spilling (10).

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Water-soluble contrast appears to cause more pain because it distends the fallopian tubes and uterus more rapidly than the high-viscosity oil-soluble media (5,11). Another hypothesis is that pain is felt secondary to release of local prostaglandins, which result in uterine cramps. The pain is conducted by the pelvic splanchnic nerves from the cervix and lower part of the uterus, whereas pain from the fundus and the body of the uterus is conducted by hypogastric nerves (12). The prevalence of pain also differs according to the injection device used and the examiner’s technique (13).

In routine practice, four analgesic procedures are used to prevent pain perception during HSG. These are: use of oral nonsteroidal anti-inflammatory drugs (NSAIDs) for systemic pain medication; paracervical block for the cervical pain mechanism; application of topical analgesic cream to the uterine cervix; and intrauterine analgesic instillation for the uterine-tubal pain mechanism. Many studies have been performed in various countries regarding pain relief during HSG, and these procedures have been shown to decrease pain to some degree during HSG and sonohysterography (10,14-16). However, all of these studies have highlighted the effectiveness of different analgesic techniques in comparison with placebo-control groups. To the best of our knowledge, there has been no study that has directly compared these four analgesic techniques. Also, the most painful phase in the procedure was not determined in the previous studies (10,17,18).

The present study was performed to compare the effects of different analgesic methods during HSG to identify an effective analgesic modality for pain relief. In the current study, we aimed to investigate, in addition to an NSAID, which of three analgesic methods would be most effective in reducing discomfort associated with HSG in a prospective, randomized, controlled study. We also aimed to investigate the most painful phase in the HSG procedure and, therefore, to inform the patient about this step for psychological preparation and management of any anxiety.

METHODS

The present prospective, randomized study was performed between May and August 2013 at the Department of Obstetrics and Gynecology, Kocatepe University, Afyonkarahisar, Turkey. Ethics approval was obtained from the Institutional Review Board. Experimental procedures followed the ethical standards for experimentation on humans established by the Declaration of Helsinki of 1975, revised in 1983.

Participants

All patients admitted to the authors’ infertility clinic were evaluated for appropriateness of participation in the study, and those who met the enrollment criteria were invited to participate. Informed consent was obtained from subjects who underwent HSG during infertility assessment. A total of 80 women were recruited for the present study using a convenience sampling method. Subsequently, a total of five patients declined to participate in the study without providing a reason. These five women were excluded, and the remaining 75 patients were randomly divided into four groups.

The groups received naproxen sodium (group 1), naproxen sodium + paracervical block (1% lidocaine) (group 2), naproxen sodium + paracervical analgesic cream (5% lidocaine) (group 3), or naproxen sodium + intrauterine analgesic instillation (1% lidocaine) (group 4).

Subjects were given prophylactic antibiotics before the procedure. The 75 women in all four groups were instructed to self-administer a single oral dose of 550 mg of naproxen sodium 1 h before the scheduled time of the procedure. Subsequently, women in group 1 received no additional medication for pain relief.

In group 2, 6 mL of 1% lidocaine (2 mg/kg to 4 mg/kg), a local anesthetic drug, was injected into the cervix in divided doses of 1.5 mL circumferentially at 12, 4, 6 and 8 o’clock positions; 5 min was allowed to elapse before proceeding with the HSG.

In group 3, the posterior vaginal fornix was filled with 3 mL of 5% lidocaine cream (Anestol Pomad, Sandoz Pharmaceuticals, Germany). The cream was applied by a doctor to the fornix using a vaginal speculum 30 min before the procedure.

In group 4, women received an intrauterine instillation of 5 mL of 1% lidocaine 2 min before the procedure.

Exclusion criteria

Patients who had known stenotic cervical os; acute cervicitis; intense anxiety; a history of any allergy to local anesthetics, radio-opaque dye or anti-inflammatory medications; any recent history of acute pelvic inflammatory disease; any vaginal discharge (known to exacerbate and flare up following HSG); any other cause of chronic pelvic pain; a positive β-human choriongonadotropin test; or were <18 years of age were excluded. All participants were 18 to 40 years of age and married.

Procedure

The HSG was performed in the same room, on the same table and with the same technique by only two gynecologists to maintain consistency and limit confounding variables.

The HSG procedure was performed while the women were in a dorsal lithotomy position. A sterile metal speculum was used to visualize the uterine cervix. Antiseptic 1% chlorhexidine solution was used to wash the vagina and cervix. For groups 1 and 3 immediately and groups 2 and 4 (intracervical block with lidocaine and intrauterine instillation of lidocaine, respectively) 5 min and 2 min, respectively, before the procedure, a single-toothed tenaculum was placed on the anterior lip of the cervix transversely. A metal cannula was gently inserted into the external cervical os, the cannula and tenaculum were secured together, and the speculum was removed. Traction was placed on the tenaculum, and 15 mL to 20 mL of water-soluble iodinated contrast media (a compound of iohexol [Omnipaque 350 mg/50 mL, Opakim, Turkey]), was instilled slowly via the cannula to prevent pain while the necessary images were obtained. After the procedure, the instruments were removed and the patient was observed for 15 min to 30 min in the clinic.

Measures

In all groups, the pain during the procedure was scored at five consecutive steps: step 1, before beginning the procedure (for baseline pain perception); step 2, just after speculum insertion; step 3, at the time of placement of the tenaculum; step 4, just after instillation of the liquids used for HSG; and step 5, 15 min after the HSG was completed and instruments removed.

At each stage of the procedure, patients were asked to rate their pain during HSG using a 0 cm to 10 cm visual analogue scale (VAS, 0 = no pain, 10 = worst possible pain). VAS scores were measured and recorded in real time by the same radiology technician.

Procedure time was calculated as the time between the placement of the tenaculum and the end of the procedure after the tenaculum and cannula were removed by the same radiology technician.

Statistical analysis

Original research articles in the literature were analyzed before the sample size was calculated, but none of the articles compared the three topical anesthetics among groups. The study by Bachman et al (20) was used for the calculations, with a difference of at least 1.3 on a VAS with a highest SD of 1.2 being regarded as clinically significant (α=0.05, power = 0.80), and a sample size of at least 14 in each group. A one-way ANOVA test was used for analysis. If variances were determined to be homogeneous, the Tukey honest significant difference test was used; if variances were nonhomogeneous, the Tamhane test was used. Proportions were assessed using cross-tabulation, and the χ² test was used to compare these proportions in different groups. Values are presented as mean ± SD, and for categorical variables as n (%). If P<0.05, the difference was considered to be statistically significant.

RESULTS

A total of 75 patients were included in the present study, and were randomly assigned to four groups (Figure 1). Group 1 received 550 mg naproxen sodium (n=20), group 2 received 550 mg naproxen sodium +
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Patient age, weight, height, obstetric history, education and procedure time were not significantly different among groups (Table 1). There was no correlation between education level and pain perception (P>0.05). The preprocedure VAS scores of all four groups were not significantly different (P>0.05).

There were no differences in terms of pain scores among groups (P>0.05) before beginning the procedure (step 1, as the point of baseline pain perception) (0.7±0.3, 0.5±0.1, 0.16±0.3, 0.02±0.04, groups 1 to 4, respectively), just after speculum insertion (step 2) (1.3±1.1, 1.3±0.62, 1.2±0.8, 0.4±0.8, groups 1 to 4, respectively), at the time of placement of the tenaculum (step 3) (3.9±1.4, 3.2±1.1, 2.8±1.6, 2.7±1.5, groups 1 to 4, respectively) and 15 min after the HSG was completed and instruments removed (step 5) (0.8±1.8, 0.2±0.3, 0.3±0.7, 0.3±0.5, groups 1 to 4, respectively) (Table 2).

Instillation of the liquids used for HSG was found to be the most painful step of HSG; this step is where the only significant difference among groups was found (P<0.001) (Table 2). Pain perception in step 4 was significantly higher in group 1 compared with group 2 (7.2±1.6 versus 4.7±2.5, respectively; P<0.001). In step 4, a difference was found between group 2 and group 4, which was not as high as for the previous groups; nevertheless, this was also statistically significant (4.7±2.5 versus 6.7±1.8, respectively; P<0.001). There was also a significant difference between group 1 and group 3 (7.2±1.6 versus 4.7±2.5, respectively; P<0.001). In step 5, no differences were observed between groups 2 and 3 (4.7±2.5 and 3.8±2.4, respectively; P=0.4).

DISCUSSION

The most important finding of the present study was that local application of lidocaine cream to the posterior fornix of the cervix uteri and lidocaine injection into the cervix uteri at four different points during HSG effectively reduced pain during the procedure. However, this pain reduction effect was limited to immediately after instillation of the liquids used for visualization of the uterine cavity and fallopian tubes (step 4). Other steps of the procedures were similar in terms of pain perception according to VAS for all methods. Also, we found that step 4 was the most painful phase in the procedure; this step is where a significant difference among groups was found.

HSG is typically performed as part of an infertility work-up or in the evaluation of recurrent early pregnancy loss, and rarely to confirm tubal occlusion after surgical sterilization. The most frequent side effect of HSG is pain. Fortunately, it is short-lived, but up to 72% to 80% of patients report mild to moderate pain during the procedure (7,8). Because of this side effect, many different methods have been used to prevent pain perception during HSG. These include oral, intravenous and topical analgesics (10,14,15,17-23). To the best of our knowledge, our study is unique in being the first study comparing different methods to prevent pain perception during HSG.

According to Duffy et al (24), in a national survey study from the United Kingdom, nonopioid analgesia (acetaminophen, acetylsalicylic acid and fenoprofen) was the most preferred prophylactic analgesic method, being offered by 52% of clinicians to patients for the prevention of pain during the HSG procedure. A Cochrane review reported that at both up to 29 min after the procedure and >30 min after the procedure, the beneficial effects of using a nonopioid analgesic over a placebo could not be demonstrated (25). In our study, we found that group 1 had the highest VAS pain score in all steps of the HSG procedure; this finding was consistent with these studies.

According to some authors, intracervical block is believed to be the most effective method. The use of this technique for pain relief in the HSG procedure was first studied by Robinson et al (10) in 2007. According to their results, patients can tolerate pain during tenaculum placement and tenaculum traction during a HSG with intracervical block better than placebo, but this pain-relieving effect was not present for pain perception during the most painful component of the HSG, which was the instillation of contrast into the uterus. Thus, the authors concluded that intracervical block should be offered to all patients undergoing HSG with NSAIDs. A second study investigating intracervical block effectiveness in HSG procedures was performed.
In this study, the main difference from the Robinson et al (10) study was that the analgesic effect was observed at all stages of the process, even during instillation of dye and 1 min after completion of the process and removal of the instruments. Chauhan et al (22) explained this difference as due to premedication drugs. In contrast to the Robinson et al (10) study, Chauhan et al (22) used intramuscular atropin and promethazine hydrochloride 30 min before the procedure as premedication, which was not given in the study performed by Robinson et al, in which 800 mg ibuprofen was given orally 30 min before the procedure. Interestingly, our study showed that intracervical pain block (group 2) was effective during instillation of dye compared with during placement of the tenaculum (better than the control but not significant). Although we used a similar premedication as in the Robinson et al study, our results showed no similarities to their findings. Contradictions between previous studies and our study are clearly apparent. In addition, a meta-analysis by Tangsirinwathana et al (26) concluded that there is no definitive evidence that paracervical block is better or worse than alternative analgesic techniques in terms of efficacy for women undergoing uterine interventions.

The other technique investigated for pain relief during the HSG procedure was local application of lidocaine cream to the posterior fornix of the cervix uteri plus oral NSAID. In all groups in our study, the best results for VAS scores in step 4 were obtained in this study group. According to Liberty et al (17,18), insertion of cervical instruments was the most painful step during the HSG procedure. There have been only two previous randomized controlled studies comparing local anesthetic application to cervix uteri with placebo during HSG (17,21). Lorino et al (21) conducted a study in which 20% benzoic acid gel was applied to the uterine cervix in one group of women, who were then compared with a group who received a placebo. The authors found a significant reduction in pain during HSG with topical benzoic acid gel. In another study, it was demonstrated that topical application of 5% lidocaine-prilocaine cream to the uterine cervix before HSG significantly reduced the pain associated with this procedure (17). Based on this work, we suggest that if the pain score is unchanged between speculum insertion and contrast media instillation via catheter (except after application of the tenaculum and the cannula on the uterine cervix), then the administered pain relief method is successful. In the literature, most studies observed pain to vary during different steps of the treatment process. Pain perception was not perceived as being the same during speculum insertion compared with uterine filling or tubal spilling.

According to Liberty et al (17), cervical instrument insertion was the most painful step in the HSG procedure. We suggest that awareness of the most painful phase during the HSG procedure is especially important for psychological preparation of the patient before this step so that anxiety can be managed.

| Step | Group 1 | Group 2 | Group 3 | Group 4 | P |
|------|---------|---------|---------|---------|---|
| 1    | 0.17±0.3 | 0.05±0.1 | 0.16±0.3 | 0.02±0.04 | >0.05 |
| 2    | 1.3±1.1  | 1.3±0.62 | 1.2±0.8  | 0.4±0.8  | >0.05 |
| 3    | 3.9±1.4  | 3.0±2.1  | 2.8±1.6  | 2.7±1.5  | >0.05 |
| 4    | 7.2±1.6  | 4.7±2.5  | 3.8±2.4  | 6.7±1.8  | <0.001*†‡§¶ |
| 5    | 0.8±1.8  | 0.2±0.3  | 0.3±0.7  | 0.3±0.5  | >0.05 |

Data presented as mean ± SD unless otherwise indicated. One-way ANOVA test was used; differences were considered to be statistically significant at P<0.05. Step 1: Before beginning the procedure (as point of base-line pain perception); step 2: Just after speculum insertion; step 3: At the time of placement of tenaculum; step 4: Just after instillation of the liquids used for hysterosalpingography; step 5: 15 min after the HSG completed and instruments removed. Group 1: 550 mg naproxen sodium; group 2: 550 mg naproxen sodium + paracervical analgesic cream; group 3: 550 mg naproxen sodium + paracervical block; group 4: 550 mg naproxen sodium + intrauterine analgesic instillation. *P<0.001 for group 1 versus group 2; †P<0.001 for group 1 versus group 3; ‡P=0.4 for group 2 versus group 3; §P=0.02 for group 2 versus group 4; ¶P<0.001 for group 3 versus group 4.
the uterine cavity and fallopian tubes (step 4) was the most painful step in the procedure.

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