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Research Article

Predictors of Pain Associated With Hysterosalpingography (HSG): A Prospective Cohort Study

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Abstract

Predictive factors of pain were evaluated prospectively in a cohort of 157 women undergoing hysterosalpingography (HSG). 94% of women experienced pain associated with the procedure. A history of dysmenorrhea or tubal obstruction at time of procedure was a significant predictor of increased pain associated with HSG. Pre-procedure treatment with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) was not associated with changes in pain scores.

Objective: To identify predictive factors of pain associated with Hysterosalpingography (HSG).

Design: Prospective cohort study.

Setting: Academic medical center.

Patients: 157 consecutive women undergoing HSG as part of infertility evaluation.

Interventions: Completion of standardized pre- and post-procedure questionnaires, including Post-Procedure Visual Analog Scale (VAS), Present Pain Intensity (PPI) and Short Form McGill Pain Questionnaire (SF-MPQ)

Main Outcome Measures: Prevalence and nature of HSG-associated pain, VAS, PPI and SF-MPQ results, predictors of HSG-associated pain.

Results: Of the 157 women undergoing HSG, 94% of patients experienced pain during the procedure. Not surprisingly, the most common description of the nature of pain was "cramping" (86.5%). The severity of reported pre-procedure dysmenorrhea was statistically significantly associated with the occurrence of HSG-associated pain ($r=0.315$, $p<0.01$). Additionally, women with tubal obstruction experienced a significant increase in HSG-associated pain ($p=0.011$). Patients using pre-procedure non-steroidal anti-inflammatory drugs (NSAIDs, 85.4% of women) experienced no significant decreases in VAS pain scores (73.7 versus 82.0, $p=0.40$).

Conclusion: The majority of women experience pain during HSG. A history of dysmenorrhea and a finding of tubal obstruction were statistically significant predictors of HSG-associated pain.Pre-procedure treatment with NSAIDs reduced pain scores, however this was not statistically significant.

Keywords: Hysterosalpingography; HSG; Visual Analog Scale; Short Form McGill Pain Questionnaire; Dysmenorrhea; Non-Steroidal Anti-Inflammatory Drugs

Introduction

The workup of the infertile patient commonly consists of a battery of tests designed to identify the cause of infertility. Hysterosalpingography (HSG) is a first-line investigation in the evaluation of infertility to assess tubal patency and uterine cavity contour [1,2]. The vast majority of women experience pain during the HSG procedure [3]. Despite its common use, little information is available regarding the characteristics of HSG-associated pain, factors predisposing to increased pain experience, and methods to decrease pain experienced during the procedure. Various strategies to reduce HSG-associated pain have been proposed and studied [4-8]. However, risk factors for the occurrence of HSG-associated pain have not been established.

Understandably, the infertility workup can be a cause of anxiety for many patients. The pain associated with HSG may contribute to the negative experience in the infertility workup. The primary aim of this study was to identify predictors of pain associated with hysterosalpingography in a prospective fashion. The secondary aim was a quantitative and qualitative description of the presence, character and severity of HSG-associated pain. With a better understanding of pain characteristics, women may be better counseled on what they may experience during their HSG. Additionally, identifying predisposing

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factors may give us a better understanding of the pathophysiology of HSG-associated pain and lead to future advances in this area.

Materials and Methods

The University of Oklahoma Health Sciences Center (OUHSC) Institutional Review Board approved this study. During the study period of February 1, 2010 to March 1, 2011, all women who met the inclusion and exclusion criteria were invited to participate in the study. Inclusion criteria were: age ≥18 and undergoing clinically indicated HSG for evaluation of infertility or recurrent pregnancy loss. Exclusion criteria were: age <18, and patients who declined participation in the study.

HSG procedure

Prior to scheduling the procedure, participating women were given an HSG educational handout from the American Society for Reproductive Medicine(ASRM) providing information about the procedure and advising patients to take an oral medication for menstrual cramps prior to the procedure [9]. On the reverse side of the provided patient fact sheet, the specific recommendation was made that she take an NSAID (Ibuprofen 400-800 mg po or Naproxen 220 mg) one hour prior to the procedure, although this was not required. All HSGs were performed on an outpatient basis by a general gynecologist or a reproductive endocrinologist. In lithotomy position, a speculum was placed in the vagina and an iodine solution was applied to the cervix. The anterior lip of the cervix was then injected with 1-2 ml of 0.5% lidocaine, and a tenaculum placed. A transcervical acorn cannula was placed into the area near the internal os. Five to 20 ml of the water-soluble nonionic radio-opaque dye Iopamidol (Isovue; Bracco Diagnostics Inc., Princeton, NJ) was injected under fluoroscopic visualization. Multiple radiograph films were obtained.

Standardized questionnaires

Immediately prior to the HSG procedure, participants were asked to complete an anonymous, coded health questionnaire to collect demographic data and information on obstetric and gynecologic history, including prior pregnancies and mode of delivery, menstrual history, and any prior gynecologic diagnoses. Data on pre-procedure NSAID use was also collected. Within 10 minutes of completing the HSG procedure, participants were asked to complete an anonymous, coded pain questionnaire.In order to characterize pain quality ,intensity, and overall experience the questionnaire contained three tools: the McGill Pain Questionnaire- Short Form" (MPQ-SF), a Visual Analog Scale (VAS) and the Present Pain Intensity (PPI) index. Nominal data was collected from the MPQ-SF and PPI pain tools, and continuous data was collected from the VAS.

Pain characteristics were recorded using the MPQ-SF, as described by Melzack et al. [10]. The MPQ-SF included 15 word descriptors of pain rated on a scale 0 to 3, (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain). The first 11 descriptors refer to sensory quality of the pain experience. The final 4 descriptors relate to the affective dimension of the pain. The scale has been found to be valid, reliable, and repeatable in a variety of acute and chronic conditions [11,12].

The VAS consisted of a 100-mm horizontal line with anchors of "no pain" on the left and "the most intense pain imaginable" on the right. Patients indicated the maximum pain intensity experienced during the HSG by making a vertical line on the VAS. The VAS pain measurement tool has been used extensively and it has been validated for quantitative pain assessment in a variety of settings [13,14].

The final scale completed by the subject was the PPI Index, an overall assessment of the pain experienced during the HSG. The PPI is a powerful overall intensity score, provided by the numerical value associated with the five verbal descriptors which are psychologically equally distant from each other (0 = No pain, 1 = Mild, 2 = Discomforting, 3 = Distressing, 4 = Horrible, 5 = Excruciating) [10].

Following the HSG procedure, the performing physician documented results and details of the procedure, including instruments used and use of topical cervical anesthetic on a de-identified, coded form that could be linked only to the questionnaires completed by the subject. Tubal patency and anatomy of the fallopian tubes and uterus were also recorded.

Statistical analysis

Pain scores reported by VAS and PPI were reported as mean ± standard error.

TheMann-Whitney Uand Kruskal-Wallis tests were used to compare non-parametric continuous and nominal measures (PPI and MPQ-SF), and Spearman correlation coefficients were calculated to correlate predictors of pain with the VAS and PPI results.SAS Statistical software was used for analysis (SAS version 9.2, Cary, NC). A p value of ≤0.05 was considered statistically significant.

Results

One hundred fifty-seven participants met the inclusion and exclusion criteria and consented to study. The mean age of participants was 30.8 ± 3.1 years. The majority of subjects were Caucasian (74.5%). Demographic information, pain quantity as assessed by VAS, quality of pain as assessed by MPQ-SF, pre-procedure use of analgesia, and study results are described in Table 1.

Table 1: Baseline characteristics of the study population.

Variable		Study population (n=157)
Age, yrs (Mean ± SD)		30.8 ± 3.1
Ethnicity (n, %)		
	Caucasian	118 (75.2%)
	Hispanic	15 (9.6%)
	African-American	14 (8.9%)
	Native American	6 (3.8%)
	Asian	4 (2.5%)
Nulliparity (n,%)		102 (65.0%)
Prior HSG (n,%)		22 (14.0 %)
Cycle length (days, Mean ± SD)		28.6 ± 4.1
Duration of menses (days, Mean ± SD)		4.0 ± 1.3
History of Dysmenorrhea (n%)		
	None	14 (8.9%)
	Mild	66 (42.0%)
	Moderate	50 (31.8%)
	Severe	27 (17.2%)

Table 2: Univariate correlation between baseline parameters and objective pain score (as assessed by VAS).

Parameter	Rho (Spearman correlation coefficient)	p-value
Age	-0.13	0.26
Cycle length	0.05	0.57
Duration of menses	0.24	0.003
Quantitative assessment of dysmenorrhea	0.32	<0.001
Infertility duration	0.04	0.65
Gravidity	0.035	0.67

Pain was experienced by 94% of subjects. The SF-MPQ required participants to qualify their pain within 15 word descriptors. The most frequent and intense pain descriptors were "cramping" (86.5% of subjects; 1.65 ± 0.08 mean score ± standard error), "aching" (46.6%; 0.76 ± 0.008), "heavy like a weight" (44.4%; 0.72 ± 0.08), and "sharp" (51%; 0.94 ± 0.1). Seventy-six percent of subjects experienced at least "moderate pain" for one or more of the pain descriptors and 22% experienced "severe pain" for one or more of the pain descriptors. Mean score using VAS was 38.9 ± 26.6. Mean PPI was 2.08 ± 0.99. The VAS and PPI were strongly correlated (r=0.63; p<0.0001).

Of the demographic and clinical variables assessed, only a history of dysmenorrhea was significantly correlated with pain during HSG as measured by VAS. The likelihood of experiencing pain with HSG increased as women reported a history of more severe dysmenorrhea (p=0.0001, r=0.315). Age, cycle length, duration of infertility, gravidity, and parity were not significantly correlated with pain as assessed by VAS. Table 2 is a summary of the Spearman univariate correlation coefficients between baseline parameters and objective pain score (as assessed by VAS). The mean (± standard deviation) objective pain scores (as assessed by VAS) by clinical parameters are shown in Table 3.

Of the 157 subjects, 134 (85.4%) used oral analgesia prior to HSG. The mean VAS score for patients who took pre-procedure analgesia, and those who did not was 73.73 and 81.98, respectively, (p=0.399). All but 3 study participants received lidocaine for cervical block, with no statistically significant difference in pain scores. Of the 1576 patients, 146 (93.06%) reported receiving pre-procedure counseling about the HSG procedure by a physician. A trend towards lower pain scores following physician counseling was observed in the study, but this was not statistically significant.

A finding of tubal obstruction at the time of the procedure was positively correlated with experience of pain (p=0.011). A finding of uterine anomalies was not correlated with pain associated with hysterosalpingography (p=0.469).

Discussion

A great majority of patients undergoing HSG experience pain in some form associated with the procedure. Studies evaluating pain are complicated by the subjective nature of pain; it is difficult to systematically record pain perception in a reliable and reproducible manner. In this study we used the MPQ-SF for pain assessment, which has previously been demonstrated to be a highly reliable tool in assessing the multidimensional experience of pain [11]. We attempted to identify potential predictors of HSG-associated pain. Candidate predictors were demographic and clinical variables such as parity, a history of dysmenorrhea, and previous pelvic surgeries, as well as procedure-related factors such as oral pre-medication, and HSG findings such as tubal obstruction.

Table 3: Objective pain scores (as assessed by VAS) by clinical parameters.

Clinical Parameter		VAS score (Mean ± SD)	p-value
Physician counseling	Yes	38.05 ± 27.98	0.51
	No	44.77± 32.35	
Analgesia use	Yes	37.48 ± 26.95	0.40
	No	43.30 ± 32.03	
Operator performing HSG	A	39.81 ± 27.40	0.054
	B	42.71 ± 27.78	
	C	31.36 ± 25.72	
	D	73.68 ± 38.55	
History of tubal obstruction	Yes	51.90 ± 32.63	0.011
	No	36.13 ± 26.08	
History of known uterine cavity abnormalities	Yes	40.42 ± 27.79	0.47
	No	36.69 ± 31.00	
History of sexually transmitted disease	Yes	20.48 ± 26.47	0.16
	No	40.52 ± 27.99	

This study demonstrates that a history of dysmenorrhea, especially severe dysmenorrhea, was significantly correlated with pain during HSG as measured by VAS. We hypothesize that patients with a history of dysmenorrhea may be more acutely sensitive to prostaglandin release during the HSG procedure. Age, cycle length, duration of infertility, gravidity, and parity were not significantly correlated with HSG-associated pain. Our finding that a history of dysmenorrhea predicts HSG-associated pain may assist providers in counseling prior to the HSG procedure.

Pre-procedure oral NSAID analgesia did reduce HSG-associated pain scores, although this finding was not statistically significant. An explanation for this finding could be that almost all study participants received lidocaine for cervical block, potentially providing most of the anesthetic effect. Numerous previous studies have addressed the effectiveness of local anesthetic use during HSG. A randomized controlled trial by Frishman et al. from 2004 including 64 subjects found no statistically significant reduction in pain for the group randomized to intrauterine lidocaine during HSG versus placebo [6]. Karasahin et al. did report effective pain control using topical lidocaine spray [8]. A randomized, controlled trial on 120 patients found significantly reduced VAS scores in those randomized to lidocaine intracervical block during HSG compared to placebo [15]. In a recent prospective trial on HSG-associated pain from India, 100 women were randomized to intracervical block plus oral premedication versus oral premedication alone [16]. Significant reductions in procedure-associated pain as measured by VAS were observed in the intervention group. The authors of both studies concluded that intracervical block should be routinely offered to all women undergoing HSG. Therefore, the effect of added oral pre-medication may have been too small to detect in our study.

While our study did not reach statistical significance for the reduction of pain with oral pre-medication, other studies have specifically addressed this issue. Hassaet et al. [17] demonstrated a statistically significant decrease in pain experienced during HSG in women pretreated with NSAIDs versus a control group and misoprostol. Although they did identify a decrease in pain experience

during the procedure, pain scores at 30 minutes post-procedure were not statistically significant. Bello et al. studied tramadol as prophylaxis in African women [5]. In their study, premedication with tramadol failed to decrease pain as compared to placebo. Anserini and colleagues demonstrated that NSAID premedication did not significantly reduce pain experienced by study subjects as compared to placebo [4]. They did note, however, that HSG is generally a well-tolerated procedure. Likewise, Guzelet et al. showed no significance difference in pain experienced between those treated with flurbiprofen and those treated with placebo [7]. Although there is conflicting data, the current standard of care is to suggest pre-procedure oral anti-inflammatory medication prior to HSG.

Although 94% of women experienced some pain during the HSG procedure, the average VAS score was only 38.9 with 100 being the most intense pain imaginable. The average PPI score was 2.08 on a scale of 0 to 5 (0 = No pain, 1 = Mild, 2 = Discomforting, 3 = Distressing, 4 = Horrible, 5 = Excruciating). On average patients described the procedure as "discomforting". Therefore, the majority of females undergoing HSG can be reassured that they will likely experience only mild to moderate discomfort. Identification of factors predicting a higher likelihood of the occurrence of moderate or severe levels of pain would allow physicians to counsel patients on a more individual basis. This type of counseling may improve patient expectations and hence satisfaction with the procedure, and help decrease discomfort. In our study, decrease in pain following physician counseling did not reach statistical significance. However, only 10 patients were not counseled prior to HSG, and lack of knowledge about risk factors may be responsible for inadequate pre-procedure counseling.

Higher pain scores were experienced by patients subsequently found to have tubal obstruction, but not by patients found to have uterine anomalies. These findings may assist with more individualized counseling. Patients at high risk for tubal occlusion should be counseled that they may experience more pain during the procedure.

HSG is an essential part of the infertility workup [2]. As such, it is commonly performed. Our study demonstrates that most women experience pain associated with the procedure, most frequently described as cramping. Continued basic scientific research is necessary to identify predictors of HSG-associated pain and measures that are effective in alleviating procedure-related discomfort.

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