

Sonohysterographic screening before in vitro fertilization

Alexis H. Kim, M.D., Heather McKay, M.D.,* Martin D. Keltz, M.D.,†
H. Preston Nelson, M.D., and G. David Adamson, M.D.

Fertility and Reproductive Health Institute of Northern California, San Jose, California

Objective: To evaluate the use of sonohysterography for uterine screening before IVF

Design: Prospective screening with sonohysterography and comparison with available hysterosalpingographic and hysteroscopic evaluations

Setting: Private practice

Patient(s): Seventy-two women undergoing IVF-ET using their own or donor eggs.

Intervention(s): Sonohysterography was performed by instilling saline into the uterine cavity through an intracervical balloon catheter; there was concurrent vaginal sonographic visualization in all cases.

Main Outcome Measure(s): Sonohysterographic findings and pregnancy rates.

Result(s): Cavitory lesions were detected in 8 (11.1%) of 72 sonohysterographic examinations. Six of 8 cases were confirmed and treated by hysteroscopy. After sonohysterographic evaluation, 35 (48.6%) of 72 patients conceived, resulting in 25 ongoing or delivered pregnancies, 5 chemical pregnancies, and 5 spontaneous abortions. No statistically significant difference was observed in the pregnancy outcome for patients undergoing IVF who had sonohysterography compared with that for patients undergoing IVF during the same period who previously had a uterine evaluation by a different method. The estimated cost savings per patient undergoing sonohysterography instead of in-office hysteroscopy was \$275.

Conclusion(s): Sonohysterography offers advantages over in-office hysteroscopy and hysterosalpingography for evaluation of the uterus before IVF (Fertil Steril® 1998;69:841-44 ©1998 by American Society for Reproductive Medicine.)

Key Words: Sonohysterography, in vitro fertilization, hysteroscopy, hysterosalpingography

Received September 5, 1997; revised and accepted December 3, 1997.

Presented at the 45th Annual Meeting of the Pacific Coast Fertility Society, Indian Wells, California, April 10-13, 1997.

Reprint requests and present address: Alexis H. Kim, M.D., 540 University Avenue, Suite 200, Palo Alto, California 94301 (FAX: 650-322-1730).

* Queen's University, Kingston, Ontario, Canada.

† Department of Obstetrics and Gynecology, St. Luke's-Roosevelt Hospital Center, New York, New York.

0015-0282/98/\$19.00
PII S0015-0282(98)00045-4

Structural abnormalities of the uterus and endometrial cavity may affect reproductive outcome adversely by interfering with implantation and causing spontaneous abortion (1). In women undergoing IVF treatment, the incidence of uterine abnormalities has been reported to range from 19%–50% (2–5). Thus, screening the uterus before proceeding with IVF has been recommended.

The preferred method for evaluating the uterus in most studies has been hysteroscopy. Frequently, hysterosalpingography (HSG) has been performed during the course of infertility evaluation before IVF. In the detection of abnormalities, however, HSG has been reported to have a low specificity (4–6) and a false-negative rate of 10% (4). Moreover, HSG is not reliable in making a precise diagnosis of abnormalities (7), and it has a high false-positive rate (8, 9).

The use of ultrasonography (US) in con-

junction with intrauterine saline infusion sonohysterography is an appealing alternative to hysteroscopy and HSG for uterine screening before IVF. Sonohysterography has been found to be highly sensitive, specific, and accurate in identifying abnormalities such as myomas, polyps, synechiae, septa, and uterine anomalies (6, 10–13).

Compared with hysteroscopy, sonohysterography is less invasive and costly, and it allows evaluation of the entire uterus and adnexa as opposed to just the uterine cavity. In comparison with HSG, sonohysterography is better tolerated, does not require the use of radiation, and provides better diagnostic accuracy. Thus, we chose to evaluate sonohysterography as the preferred screening method before IVF.

MATERIALS AND METHODS

Beginning in October 1995, 72 consecutively seen patients who were undergoing IVF

TABLE 1

Comparison of IVF outcome in patients who underwent sonohysterography and in those who did not.

Variable	Underwent sonohysterography		P value
	Yes (n = 62)*	No (n = 103)*	
Mean (\pm SEM) patient age (y)	35.5 \pm 0.4	35.8 \pm 0.4	0.57†
Transferred embryos			
Mean (\pm SEM) no. of blastomeres	4.57 \pm 0.20	4.02 \pm 0.14	0.02‡
Mean (\pm SEM) grade	1.43 \pm 0.05	1.65 \pm 0.06	0.01†
Mean (\pm SEM) no transferred	4.81 \pm 0.24	4.49 \pm 0.17	0.27†
No. of pregnancies (% of patients)	20 (35.7%)	22 (23.4%)	0.08‡

* Number of IVF cycles

† Determined by Student's *t*-test

‡ Determined by one-tailed Fisher's exact test (95% CI, 0.92–2.53)

or donor egg recipient cycles and required uterine evaluation were screened prospectively with sonohysterography. Sonohysterography was performed during the follicular phase between days 5 and 10. Patients were given doxycycline prophylaxis for 3 days, with the first dose administered the day before the procedure.

After the vagina was prepared with povidone-iodine, an H-S catheter (Ackrad Laboratories, Cranford, NJ) was placed in the cervix and a balloon was inflated to maintain its position and prevent the reflux of saline. Occasionally, the balloon was placed and inflated in the lower portion of the uterus when it would not remain in the cervix. After evaluation of the upper part of the uterus, the balloon was deflated to allow inspection of the lower uterus. This technique was used rather than placement of a tenaculum to maximize patient comfort.

Initially, the pelvis was examined by transvaginal US using a 5.0-MHz transducer (Ultramark IV; Advanced Technology Laboratories, Bothell, WA). After assessment of the dimensions and shape of the uterus, the adnexa, and the endometrial lining, sterile saline was infused into the uterine cavity during vaginal sonographic visualization at a rate sufficient to distend the uterine cavity. Sagittal and coronal views were recorded. An examination was considered normal when no cavitory lesions, distortion, or undistended regions were detected. Positive findings such as myomas that did not affect the uterine cavity were noted. The sonohysterographic findings were discussed with the patient. The consideration of further diagnostic or therapeutic interventions was based on each individual clinical situation.

The pregnancy outcome during the study period for the patients undergoing IVF who had normal sonohysterographic findings was compared with that for patients undergoing IVF during the same period who had a uterine evaluation by different method (i.e., hysteroscopy or HSG). For purposes of comparison, only IVF cycles were included.

Cycles that involved the use of frozen embryos, assisted hatching, and donor eggs were excluded. The Student's *t*-test or the one-tailed Fisher's exact test was used for statistical analysis.

RESULTS

Seventy-two patients undergoing IVF who ranged in age from 25 to 43 years were screened using sonohysterography. Eight (11.1%) cases of cavitory lesions were detected. Five cases of polyps and one case of a large blood clot were confirmed and treated by hysteroscopy. A polyp was detected in another patient, which partially prolapsed through the cervix and was removed in the office before hysteroscopy. An arcuate uterus was diagnosed in the eighth patient; this was confirmed by HSG but was not treated. Six additional patients were noted to have intramural and subserosal myomas that did not affect the cavity. However, a myomectomy was performed in one patient because of growth of the myoma and the onset of symptoms.

After sonohysterographic evaluation, 35 (48.6%) patients conceived during the study period. In some patients, these pregnancies occurred after multiple IVF cycles, frozen embryo cycles, and spontaneous conceptions between cycles. The patient with the arcuate uterus, 3 patients with polyps, and 4 patients with myomas conceived. Of the 35 conceptions, 5 were chemical pregnancies and 5 resulted in spontaneous abortions.

The results of the comparison between patients who had sonohysterography and those who did not are summarized in Table 1. No difference in the mean (\pm SD) patient age ($P = 0.57$) or the number of embryos transferred ($P = 0.27$) was found. A statistically significant difference was observed in the cellular divisions and the grades of the embryos at the time of transfer. The embryos in the sonohysterography group had a higher cellular division ($P < 0.05$) and grade ($P < 0.05$) than those in the

non-sonohysterography group. However, the pregnancy rates (PRs) between the two groups did not reveal a statistically significant difference (relative risk, 1.53; 95% CI, 0.92–2.53).

DISCUSSION

Evaluation of the uterus for abnormalities that may interfere with implantation and that usually are surgically correctable is an important part of the screening process before IVF treatment. Because of the relatively high incidence of uterine abnormalities in patients undergoing IVF, the routine use of hysteroscopy has been recommended for screening in an IVF program (2–5). Compared with hysteroscopy, sonohysterography offers similar diagnostic capabilities. Moreover, sonohysterography provides more information regarding the size and location of myomas (14) and can distinguish between bicornuate and septate uteri (15).

This study demonstrates that the routine use of sonohysterography for uterine screening before IVF is feasible and practical. Sonohysterography is performed easily in the office with minimal discomfort and risk of infection. All of our patients who previously underwent HSG or in-office hysteroscopy reported greatest comfort during the sonohysterographic examination. Although prophylactic antibiotics should be administered for 3 days, overt infections still may occur, even in the absence of any sonographic evidence of a hydrosalpinx (6). None of the patients in this series became infected. Nonetheless, cervical cultures should be checked and patients should be counseled about the possibility of infection.

In comparison with HSG, sonohysterography is superior for evaluation of the uterus (16), does not require the use of ionizing radiation, and eliminates the risk of an allergic reaction to iodinated contrast medium. In our practice, the procedure fee for sonohysterography is \$275 less than that for in-office hysteroscopy. The actual cost savings per patient usually is more than \$275 compared with hysteroscopy, however, because sonohysterography can be scheduled at an appropriate time for baseline examination of the ovaries before initiation of an IVF cycle. A separate US examination would have to be performed if hysteroscopy were used for uterine screening.

Because of the high specificity of sonohysterography, confirmation of normal sonohysterographic findings with hysteroscopy was not performed. All positive findings were identified correctly as determined by subsequent hysteroscopy for removal of the intrauterine lesion.

A blood clot was found in a patient with a large intramural myoma and heavy menstrual flows and could be considered a false-positive finding. Blood clots may be difficult to distinguish from polyps or adhesions, especially if they cannot be dislodged by insertion of the catheter or by pulsatile infusion of the saline. In cases in which a blood clot is

suspected but not positively identified, the patient also may be offered expectant management with a repeated sonohysterographic examination after the next menses.

Despite the low probability of a false-negative result with sonohysterography, all subtle lesions may not have been detected. Although it is unlikely, even in the event that a lesion was missed, no deleterious effect on outcome was apparent. No difference in the PRs was seen between the patients who had a normal sonohysterographic examination and the remainder of the patients who had a normal uterine evaluation by a different method.

Although no statistically significant difference in the PRs was observed between the sonohysterography group and the non-sonohysterography group, the former had a higher PR. Because there was no difference in patient age or the number of embryos transferred, this finding most likely is a reflection of the better-quality embryos (grade and progression of cellular division) that were produced and transferred in the sonohysterography group. Patient selection bias probably is responsible for this difference in embryo quality.

Patients in the non-sonohysterography group had undergone previous uterine evaluations and more often had received previous failed infertility treatment. In contrast, patients in the sonohysterography group tended to be at an earlier stage in the infertility evaluation and treatment process. Thus, the non-sonohysterography group was preselected for patients who had a worse prognosis. The higher PR in the sonohysterography group, although not statistically significant, was consistent with the expectations.

Sonohysterography has the ability to detect subtle or mild abnormalities in the uterine cavity. The significance of these findings and their effect on fertility are unknown. There is evidence to suggest that mild alterations of the uterus may have an adverse effect on IVF pregnancy outcome (5). However, predicting decreased uterine receptivity on the basis of the size, location, and character of these abnormalities is not possible at this time. A randomized, prospective, controlled study of pregnancy outcome is required to enable more informed decisions regarding the appropriateness of treating mild defects.

In an IVF program, transvaginal US is a frequently used imaging modality. Sonohysterography is a technique that could be incorporated easily into an IVF program with minimal additional cost and training for use in uterine screening. Likewise, the uteri of donor egg recipients could be screened before ET. The practicality, accuracy, and relative comfort of sonohysterography confers significant advantages over HSG and hysteroscopy. Although hysteroscopy has been the traditional procedure for uterine screening before IVF, its invasiveness, cost, and discomfort may favor the use of sonohysterography. Thus, we recommend the

non-sonohysterography group. However, the pregnancy rates (PRs) between the two groups did not reveal a statistically significant difference (relative risk, 1.53; 95% CI, 0.92–2.53).

DISCUSSION

Evaluation of the uterus for abnormalities that may interfere with implantation and that usually are surgically correctable is an important part of the screening process before IVF treatment. Because of the relatively high incidence of uterine abnormalities in patients undergoing IVF, the routine use of hysteroscopy has been recommended for screening in an IVF program (2–5). Compared with hysteroscopy, sonohysterography offers similar diagnostic capabilities. Moreover, sonohysterography provides more information regarding the size and location of myomas (14) and can distinguish between bicornuate and septate uteri (15).

This study demonstrates that the routine use of sonohysterography for uterine screening before IVF is feasible and practical. Sonohysterography is performed easily in the office with minimal discomfort and risk of infection. All of our patients who previously underwent HSG or in-office hysteroscopy reported greatest comfort during the sonohysterographic examination. Although prophylactic antibiotics should be administered for 3 days, overt infections still may occur, even in the absence of any sonographic evidence of a hydrosalpinx (6). None of the patients in this series became infected. Nonetheless, cervical cultures should be checked and patients should be counseled about the possibility of infection.

In comparison with HSG, sonohysterography is superior for evaluation of the uterus (16), does not require the use of ionizing radiation, and eliminates the risk of an allergic reaction to iodinated contrast medium. In our practice, the procedure fee for sonohysterography is \$275 less than that for in-office hysteroscopy. The actual cost savings per patient usually is more than \$275 compared with hysteroscopy, however, because sonohysterography can be scheduled at an appropriate time for baseline examination of the ovaries before initiation of an IVF cycle. A separate US examination would have to be performed if hysteroscopy were used for uterine screening.

Because of the high specificity of sonohysterography, confirmation of normal sonohysterographic findings with hysteroscopy was not performed. All positive findings were identified correctly as determined by subsequent hysteroscopy for removal of the intrauterine lesion.

A blood clot was found in a patient with a large intramural myoma and heavy menstrual flows and could be considered a false-positive finding. Blood clots may be difficult to distinguish from polyps or adhesions, especially if they cannot be dislodged by insertion of the catheter or by pulsatile infusion of the saline. In cases in which a blood clot is

suspected but not positively identified, the patient also may be offered expectant management with a repeated sonohysterographic examination after the next menses.

Despite the low probability of a false-negative result with sonohysterography, all subtle lesions may not have been detected. Although it is unlikely, even in the event that a lesion was missed, no deleterious effect on outcome was apparent. No difference in the PRs was seen between the patients who had a normal sonohysterographic examination and the remainder of the patients who had a normal uterine evaluation by a different method.

Although no statistically significant difference in the PRs was observed between the sonohysterography group and the non-sonohysterography group, the former had a higher PR. Because there was no difference in patient age or the number of embryos transferred, this finding most likely is a reflection of the better-quality embryos (grade and progression of cellular division) that were produced and transferred in the sonohysterography group. Patient selection bias probably is responsible for this difference in embryo quality.

Patients in the non-sonohysterography group had undergone previous uterine evaluations and more often had received previous failed infertility treatment. In contrast, patients in the sonohysterography group tended to be at an earlier stage in the infertility evaluation and treatment process. Thus, the non-sonohysterography group was preselected for patients who had a worse prognosis. The higher PR in the sonohysterography group, although not statistically significant, was consistent with the expectations.

Sonohysterography has the ability to detect subtle or mild abnormalities in the uterine cavity. The significance of these findings and their effect on fertility are unknown. There is evidence to suggest that mild alterations of the uterus may have an adverse effect on IVF pregnancy outcome (5). However, predicting decreased uterine receptivity on the basis of the size, location, and character of these abnormalities is not possible at this time. A randomized, prospective, controlled study of pregnancy outcome is required to enable more informed decisions regarding the appropriateness of treating mild defects.

In an IVF program, transvaginal US is a frequently used imaging modality. Sonohysterography is a technique that could be incorporated easily into an IVF program with minimal additional cost and training for use in uterine screening. Likewise, the uteri of donor egg recipients could be screened before ET. The practicality, accuracy, and relative comfort of sonohysterography confers significant advantages over HSG and hysteroscopy. Although hysteroscopy has been the traditional procedure for uterine screening before IVF, its invasiveness, cost, and discomfort may favor the use of sonohysterography. Thus, we recommend the