Efficiency and pregnancy outcome of serial intrauterine device–guided hysteroscopic adhesiolysis of intrauterine synechiae

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Objective: To highlight the efficiency of intrauterine device (IUD) guidance during hysteroscopic adhesiolysis for severe intrauterine adhesions.
Design: A prospective, randomized trial.
Setting: Private tertiary and referral infertility clinic.
Patient(s): Seventy-one subfertile patients who underwent hysteroscopic treatment of intrauterine synechiae or adhesions.
Intervention(s): Thirty-six women in group 1 were initially examined by laparoscopy-hysteroscopy at first look, and an IUD was inserted during hysteroscopic adhesiolysis. The adhesions were further lysed by the guidance of IUD during the second-look office hysteroscopy, 1 week later. Patients were prescribed 2 months of estrogen as well as P therapy, and the IUD was removed by the end of this period. The uterine cavity was evaluated, and adhesions were further lysed by a third-look office hysteroscopy, 1 week after the removal of IUD. Thirty-five women in group 2 were similarly examined by first-look office hysteroscopy, and an IUD was inserted during hysteroscopic adhesiolysis. These patients did not undergo early intervention of office hysteroscopy, 1 week after the first procedure. They also used 2 months of estrogen and P therapy. The IUD was removed by the end of this period, and the uterine cavity was evaluated and adhesions were further lysed during a second-look office hysteroscopy.
Main Outcome Measure(s): Pregnancy rate and live birth rate.
Result(s): Spontaneous pregnancy rates after treatment were 17/36 (47.2%) and 11/35 (30%), and live birth rates were 10/36 (28%) and 7/35 (20%) in groups 1 and 2, respectively. These differences between the two groups were not statistically significant.
Conclusion(s): The method described especially for early intervention may prevent complications during the treatment of severe intrauterine adhesions and may present a secure and effective alternative for constructive clinical outcomes. (Fertil Steril® 2008;90:1973–7. ©2008 by American Society for Reproductive Medicine.)

Key Words: Intrauterine synechiae, hysteroscopy, adhesiolysis, intrauterine device, Asherman's syndrome

Intrauterine adhesion (IUA) contributes to the etiology of both infertility and recurrent pregnancy loss (1). Intrauterine adhesion may present as secondary amenorrhea, hypomenorrhea, infertility, or obstetric complications and may result from trauma of dilatation and curettage, postabortal infection, genital tuberculosis, or previous uterine surgery (2–7). Diagnosis and treatment of IUAs are essential for the evaluation of infertility patients, including those undergoing IVF.

Currently, hysteroscopy is the most effective method of diagnosis for IUAs, because it is the intervention that is least aggressive to the healthy endometrium (8). Lysis of adhesions under direct vision presents a safer and more comprehensive technique, compared with blind curettage or hysterotomy. It is possible to sever only scar tissue and to spare normal endometrium by hysteroscopy (9). Occasionally, simply the touch of the endoscope is sufficient to eliminate IUAs. Optically controlled scissors and knives adapted for the instrument are used for dense adhesions. Hysteroscopic adhesiolysis is indicated especially for moderate to severe cases and those involving blockage of access to tubal ostia. The initial severity of adhesions may not be favorable for the complete achievement of adhesiolysis by hysteroscopy at once and may lead to complications of the procedure, including uterine perforation (10). Intrauterine devices and Foley catheters frequently are used for the maintenance of the uterine cavity and prevention of subsequent adhesion formation after adhesiolysis (5, 11).

The aim of the present report is to highlight the efficiency of the intrauterine device (IUD) in guiding the right pathway to the fundus and tubal orifices and also to compare the outcomes in two different, timely intervention groups designed to analyze the efficacy of early management after IUD insertion in severe IUAs. To our knowledge, this is the first prospective randomized study of hysteroscopic adhesiolysis

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that is performed in a number of attempts, under the guidance of the IUD.

MATERIALS AND METHODS

The current study includes 71 consecutive subfertile patients who underwent hysteroscopic treatment of intrauterine synechiae or adhesions at Centrum Clinic (Ankara, Turkey) from December 1998 to August 2005. We randomized patients sequentially, according to their entry into the study, after the study started. All patients had stage III synechiae according to the American Fertility Society classification (12). The adhesions were extensively firm, with agglutination of uterine walls and occlusion of both tubal ostial areas.

Intrauterine adhesion was diagnosed by hysterosalpingography and was confirmed by hysteroscopy in all cases. Laparoscopy was performed simultaneously with first-look hysteroscopy under general anesthesia in all patients. Infertility caused by severe male factor was excluded from the study. Etiologies for IUAs included history of at least one dilatation and curettage for elective abortion in the first trimester, at least one dilatation and curettage for missed abortion or incomplete abortion in the first trimester, a dilatation and curettage for postpartum bleeding, myomectomy involving hysterotomy, at least one dilatation and curettage for polyps or myomas, tuberculosis endometritis, cesarean delivery, and placenta accreta (Table 1). The etiologic distribution was similar among the two groups (P>.05). Of 71 patients, 23 (32%) had amenorrhea, 30 (42%) had pronounced hypomenorrhea, and 18 (25%) had recurrent pregnancy loss.

Technique

A 5-F mechanical instrument (office hysteroscope) that was equipped with hysteroscopic scissors (Karl Storz GmbH, Tuttlingen, Germany) was introduced blindly into the reduced uterine cavity. A prophylactic antibiotic, cefazolin sodium (2 g, Cefazol; Bilim, Istanbul, Turkey), was administered by the induction of anesthesia. Physiologic saline was used as the distending medium. Several cuts were performed under transabdominal ultrasound guidance with a full bladder (13). The adhesiolysis was initiated inferiorly and carried cephalad until the uterine architecture was normalized. The procedure was stopped when it was impossible to distinguish denuded myometrium from scar tissue at a stage of risk for perforation, even if ostial areas were not visible. A Lippes loop IUD was inserted to the uterine cavity at this stage of the procedure, in anticipation of further endometrial regrowth.

Patients in group 1 were initially examined by first-look office hysteroscopy, after which the IUD was inserted. The anatomical outcome was evaluated and further reconstructed by a second-look office hysteroscopy, 1 week later. The Lippes loop IUD created bits of endometrium during the regrowth of endometrium within 1 week. Briefly, endometrial bits trapped within the loops of IUD were lysed during the early intervention by second-look hysteroscopy. Interestingly, the IUD indicated the right pathway within the uterine cavity to the fundus and tubal orifices, enabling visualization of healthy endometrial cavity and both tubal orifices.

TABLE 1

Etiologies for intrauterine adhesions in the study groups.

Etiology	Group 1 (n = 36)	Group 2 (n = 35)	Total (n = 71)
D & C for elective abortion	8 (33)	6 (26)	14 (30)
D & C for missed or incomplete abortion	2 (8.3)	4 (17.3)	6 (13)
D & C for postpartum bleeding	2 (8.3)	2 (8.6)	4 (8.5)
D & C for polyps or myomas	2 (8.3)	1 (4.3)	3 (6)
Myomectomy	3 (12.5)	2 (8.6)	5 (10.5)
Tuberculosis	3 (12.5)	5 (21.7)	8 (17)
Cesarean section	3 (12.5)	3 (13)	6 (13)
Placental pathology	1 (4)	0	1 (2)

Note: Data are n (%). D & C = dilatation and curettage.

Pabuccu. IUD-guided adhesiolysis. Fertil Steril 2008.

Patients were prescribed 2 months of estrogen and P therapy, and the IUD was removed by the end of this period. Patients were evaluated by third-look office hysteroscopy 1 week after the removal of IUD.

Patients in group 2 underwent the first-look office hysteroscopy with insertion of IUD. After 2 months of estrogen and P therapy, the IUD was removed, and a second-look office hysteroscopy was performed. Patients in both groups used conjugated equine estrogen (Premarin, 5 mg; Wyeth-Ayers, Montreal, Quebec, Canada) daily and used medroxyprogesterone acetate (Farlutal, 10 mg; Deva, Istanbul, Turkey) for the last 10 days of the menstrual cycle during the 2 months of the follow-up period. Information about subsequent outcomes of fertility, including pregnancy and live birth rate, was obtained from the patients.

Statistical Methods

Statistical analyses were performed by using the χ^2 test, paired t-test, and Fisher's exact test. P<.05 was considered to be statistically significant.

RESULTS

The median (±SD) ages of women at the time of adhesiolysis were 33.2 ± 1.5 and 32.6 ± 1.6 years for groups 1 and 2, respectively (P>.05). Mean parities were 0.7 ± 0.5 and 0.6 ± 0.5 for groups 1 and 2, respectively (P>.05). Mean operating times for the initial procedure were 21.9 ± 8.2 and 20.6 ± 7.9

minutes for groups 1 and 2, respectively (P>.05). None of the patients were lost to follow-up after the control hysteroscopy. The mean follow-up time was 38 months (range, 8–67 mo) for all patients (38.4 mo for group 1 and 37.5 mo for group 2; P>.05).

The hysteroscopic intervention results in terms of adhesions were evaluated after 2 months from the initial surgery for both groups, at which time the IUD was removed as well. The results of adhesion formation are shown in Table 2. Satisfactory anatomical results, defined as no adhesion, were detected as follows: 33 (89.1%) of 36 patients in group 1 and 6 (17.1%) of 35 patients in group 2 (P<.05). There was a significant difference between group 1 and group 2 (P<.05), in that 1 week after surgery, group 1 appeared to have satisfactory results with no adhesion. When filmy, mild, and severe adhesions were compared, there was also a significant difference between group 1 and group 2, in that group 1 had better surgical results (P<.05). The comparison of group 1 and group 2 for filmy, mild, and severe adhesions was as follows: filmy adhesions, 2.7% vs. 31.3%, respectively; mild adhesions, 2.7% vs. 37%; and severe adhesions, 2.7% vs. 14.2%. Statistically, group 1 had significantly better surgical results in terms of adhesion formation. There was a significant difference in terms of adhesions between both groups (P<.05; Table 2). All of these patients were counseled to attempt pregnancy.

Spontaneous pregnancy rates after treatment were 17/36 (47.2%) and 11/35 (30%), and live birth rates were 10/36 (28%) and 7/35 (20%) in groups 1 and 2, respectively (P>.05: P=.265 and P=.624, respectively; Table 3).

In IVF-ICSI cycles after the hysteroscopic procedure, pregnancy and live birth rates, respectively, were 45% and 27% in group 1 and were 30% and 15% in group 2 (P>.05 and P>.05, respectively). Indications for IVF after adhesiolysis were male factor–oligoasthenoteratozoospermia (n = 4), tubal factor (n = 3), endometriosis stage III–IV (n = 2), advanced maternal age (n = 5), anovulation (n = 2), and unexplained infertility (n = 3).

DISCUSSION

Hysteroscopic adhesiolysis is a safe and effective procedure for the restoration of normal menstrual patterns. Most patients with amenorrhea or hypomenorrhea report improvement of symptoms after hysteroscopic adhesiolysis (8). The success rates for establishing normal menstrual patterns in patients treated for IUA are divergent in the literature. A collective series reported a success rate of 73%–92% (14–16). All patients reattained normal menstrual flow after hysteroscopic adhesiolysis in the current study. However, severe IUAs present a complex issue for clinicians to handle in patients with infertility.

The pregnancy rate after adhesiolysis may not be favorable when infertility is caused by severe IUA (Table 4). Severe adhesions may be associated with endometrial atrophy that interferes with implantation. A pregnancy rate of 43% and a live birth rate of 10% were reported in cases with severe adhesions (23). Valle and Sciarra (24) reported term pregnancy rates of 81%, 66%, and 15% in patients with infertility that was caused by mild, moderate, and severe adhesions, respectively. Pregnancy rates after the procedures were 47.2% and 30% in groups 1 and 2, respectively, in the current study. Although there were no statistically significant differences between the two groups in the study, patients in group 1 had a tendency toward increased pregnancy rates. The adhesive process can be progressive; therefore, early intervention may be essential for prognosis. Adhesions are suggested to limit uterine muscular activity, thereby reducing perfusion of sex steroids to the endometrium and leading to atrophy (9). Relatively easy procedures were performed during second-look hysteroscopies, 1 week after the first hysteroscopies. Our results may be attributed to early intervention with IUD guidance that prevented the occurrence of progressive dense adhesion that would have led to endometrial atrophy. According to the well-known healing process of fibroplasia, a measurable increase in wound tensile strength by collagen bundles does not begin before 4 to 5 days after injury (25), and before this time, the wound is held together only by weak fibrous adhesion. The time frame between wounding and the increase in

TABLE 2

Adhesion formation results.

Result	Group 1 (n = 36) One wk after hysteroscopy	Group 1 (n = 36) Two mo after hysteroscopy	Group 2 (n = 35) Two mo after hysteroscopy
None	5 (13.5)	33 (89.1)[b]	6 (17.1)
Filmy	12 (32.4)	1 (2.7)[b]	11 (31.3)
Mild	15 (40.5)	1 (2.7)[b]	13 (37.0)
Severe	4 (10.8)	1 (2.7)[a]	5 (14.2)

Note: Data are n (%).
[a] $P<.05$, statistically significant.
[b] $P<.01$, statistically significant.

Pabuccu. IUD-guided adhesiolysis. Fertil Steril 2008.

TABLE 3

Comparison of patient reproductive outcomes.

Parameter	Group 1 (n = 36)	Group 2 (n = 35)
Spontaneous pregnancies		
Pregnancy rate	17/36 (47.2)	11/35 (30)
Live birth rate	10/36 (28)	7/35 (20)
ART cycle pregnancies		
Pregnancy rate	5/11 (45)	4/13 (30)
Live birth rate	3/11 (27)	2/13 (15)

Note: Data are n (%). ART = assisted reproductive technology.

Pabuccu. IUD-guided adhesiolysis. Fertil Steril 2008.

tensile strength originally was referred to by Howes and Harwey (26) as the “lag period” of wound healing.

Application of an IUD or a Foley catheter after hysteroscopic adhesiolysis is a common therapeutic practice for maintenance of the uterine cavity. Many investigators support the use of IUDs (especially the Lippes loop) for prevention of recurrent IUAs (2, 8, 27). Copper-bearing and Progestasert (Alza Corporation, Palo Alto, CA) IUDs may have a rather small surface area and may not be able to prevent adhesion reformation. Besides, copper-bearing IUDs may induce an excessive inflammatory reaction. Loop IUDs, however, keep the raw dissected surfaces separate during the initial healing phase and reduce the chance of readherence (10, 28). Intrauterine devices and Foley catheters are used as physical means, whereas cyclic estrogen and progestins are used as medical means, for the enhancement of endometrial growth (24, 29).

We used Lippes loop IUDs for an additional purpose of guidance in transecting the precise pathway to the uterine fundus and tubal orifices during hysteroscopic adhesiolysis. An IUD-guided therapeutic approach simplifies hysteroscopic adhesiolysis for severe IUAs. The Lippes loop IUD probably enlarges the cavity and creates bits of endometrium, which simplifies the procedure for adhesiolysis. Still, maximum precaution is required during the intervention when the IUD is within the uterine cavity. The hysteroscopic procedure was repeated twice, leaving the IUD to determine its trail leisurely but safely within the uterus. Performing second-look hysteroscopy with the guidance of an IUD 1 week later can demonstrate the right pathway along which to use the scissors in the uterine cavity, toward tubal ostia. In our study, the procedure was ended when it was impossible to distinguish denuded myometrium from scar tissue. At that point, further treatment may become inefficient or dangerous, even under laparoscopic control. Therefore, endometrial regrowth was anticipated.

In addition to the IUD guidance, we also attempted abdominal ultrasonography-guided hysteroscopic division of adhesions, which provided an intraoperative sonographic view of pockets of endometrium behind an otherwise blind-ending endocervical canal in women with severe Asherman’s syndrome. This technique allowed division of adhesions under guidance and reduced the likelihood of perforations and formation of false passageways.

Adhesions also can be divided mechanically, using energy modalities such as electrosurgery and/or fiberoptic laser.

TABLE 4

Reproductive outcomes from studies elsewhere on hysteroscopic adhesiolysis, regardless of severity of Asherman’s syndrome.

Study	No. of patients	Duration of follow-up (mo)	Method of Adhesiolysis	Routine control hysteroscopy	Patients with live births (%)
Goldenberg et al. (17)	36	21.1	—	—	22.2 (8/36)
Roge et al. (18)	52	24.4	Scissors/resectoscope	—	46.1 (24/52)
Pabuccu et al. (8)	24[a]	—	Scissors/monopolar probe	—	70.8 (17/24)
	16[b]	16	Scissors/monopolar probe	—	37.5 (6/16)
McComb and Wagner (19)	5	—	Scissors	—	60 (3/5)
Protopapas et al. (20)	7	12.4 (2–30)	Knife electrode	—	28.5 (2/7)
Capella-Allouc et al. (21)	28	31 (2–84)	Monopolar knife	at 2 mo	32.1 (9/28)
Zikopoulos et al. (22)	46	39.2 ± 4.5	Resectoscope/ Versapoint system	at 2 mo	43.5 (20/46)

[a] Recurrent pregnancy loss.
[b] Infertile.

Pabuccu. IUD-guided adhesiolysis. Fertil Steril 2008.

Adhesiolysis by electroresectoscope has minimal complications (14–16). Use of the Versapoint hysteroscopic electrosurgical electrode with bipolar coagulation (Ethicon, Somerville, NJ) may be performed as an outpatient procedure (22, 29). Neither electrosurgery nor the neodymium-doped yttrium-aluminium-garnet laser offers any advantage over scissors for dissection of IUAs (9, 30).

Patients treated for moderate or severe adhesions should be considered to have high-risk pregnancies, and they should be closely monitored obstetrically, particularly to diagnose spontaneous rupture of uterus and any placental insertion abnormalities, such as placenta accreta or percreta. Complications related to placental insertion abnormalities have been shown to decrease markedly after hysteroscopic procedures, compared with the case of treatments including curettage, hysterotomy, and blind transcervical dissection (14). Severe IUA caused by genital tuberculosis also had a poor prognosis. Synechiae caused by tuberculosis were invariably cohesive and tended to recur.

Lack of data about the severity of adhesions makes the comparison of different techniques complex, according to the previous studies (Table 4). A limitation of the current study is the small sample size. However, power calculations from the results of the current study revealed that regarding the primary end point (clinical pregnancy rate per woman per cycle), a study population equal to 300 would be needed to detect any significant difference between the two groups (31).

In conclusion, hysteroscopic management of IUA is a safe and effective method that ensures lysis of all adhesions and eliminates trauma to adjacent normal endometrium. To our knowledge, this is the first report of prospective randomized hysteroscopic adhesiolysis, as performed in several steps under the guidance of an IUD. We can suggest that use of intraoperative monitoring with ultrasonography, a Lippes loop IUD, and estrogens facilitates adhesiolysis. Control hysteroscopy should be performed as early as 1 week after the initial procedure to improve the success of the procedure, which may also demonstrate a tendency for higher pregnancy rates. The method described in the current article, especially for early intervention, may prevent complications during the treatment of severe IUAs and may present a secure and effective alternative for constructive clinical outcomes.

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