

Postoperative adhesiolysis therapy for intrauterine adhesions (Asherman's syndrome)

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Objective: To evaluate postoperative blunt adhesiolysis after sharp adhesiolysis for the treatment of intrauterine adhesions.

Design: Retrospective analysis of 24 patients treated with primary hysteroscopic adhesiolysis followed by hormone therapy and serial flexible office hysteroscopy (Canadian Task Force Classification II-3).

Setting: University-affiliated community hospital.

Patient(s): Twenty-four women with menstrual disorders, pain, or infertility resulting from intrauterine adhesions.

Intervention(s): Serial, postoperative, hysteroscopic blunt adhesiolysis of recurrent synechiae.

Main Outcome Measure(s): Restoration of normal menstrual pattern, relief of dysmenorrhea, improvement in fertility, and improvement in stage of disease.

Result(s): Eighty-three percent of patients (20/24) presented with amenorrhea or oligomenorrhea, 67% (16/24) had either infertility or recurrent miscarriages, and 54% (13/24) presented with dysmenorrhea. Initially, 50% (12/24) had severe adhesions, 46% (11/24) moderate, and 4% (1/24) minimal disease according to the March criteria. Improvement in menstrual flow occurred in 95% (18/19) of patients, relief of dysmenorrhea occurred in 92% (12/13), and 46% (7/15) of fertility patients were actively pregnant or had delivered viable infants at the conclusion of the study. There was a 92% (22/24) improvement in disease staging over the treatment interval.

Conclusion(s): Blunt adhesiolysis with a flexible hysteroscope is effective for maintenance of cavity patency after primary treatment of intrauterine adhesions. (*Fertil Steril*® 2008;90:409–14. ©2008 by American Society for Reproductive Medicine.)

Key Words: Intrauterine adhesions, Asherman's syndrome, postoperative therapy, office hysteroscopy, flexible hysteroscopy

Intrauterine adhesions, or Asherman's syndrome, occur after trauma to the basalis layer of the endometrium generally after endometrial curettage. It was first described by Heinrich Fritsch in 1894 and subsequently studied by Israeli gynecologist Joseph G. Asherman. In Asherman's description, he differentiated between traumatic intrauterine adhesions, which did not typically result in menstrual disturbances, and atretic amenorrhea, which resulted in amenorrhea and dysmenorrhea due to cervical adhesions (2, 3). The syndrome occurs most frequently after incomplete abortion (50%), postpartum hemorrhage (24%), and elective abortion (17.5%) (4). Other less common etiologic factors including myomectomy, hysterotomy, diagnostic curettage, cesarean section, tuberculosis, caustic

abortifacients, and uterine packing have been reported (1, 4–7).

With damage to the basalis layer, granulation tissue on either side of the endometrial cavity can fuse to form tissue bridges. In the most severe cases, the endometrial cavity can be entirely obliterated without any evidence of viable endometrium. Patients with Asherman's syndrome may present with amenorrhea with or without severe dysmenorrhea, oligomenorrhea, infertility, or recurrent miscarriages (6). Patients with amenorrhea and cyclic pain associated with hematometria are likely to have viable endometrium above the occlusive adhesions. Sequelae of pregnancy in the presence of adhesions include higher incidences of ectopic pregnancy, recurrent miscarriage, premature labor, and abnormal placentation (8).

Valle and Sciarra demonstrated the importance of hysteroscopic management of Asherman's syndrome after reporting menstrual and fertility outcomes in 187 patients who were evaluated and treated over a 10-year period. Over 98% of these patients had undergone curettage after an initial pregnancy complication. After hysteroscopic adhesiolysis, normal menstruation was restored in 88.2% of women (4). Currently accepted treatment consists of sharp hysteroscopic adhesiolysis followed by a course of oral estrogen with subsequent P withdrawal. In cases of complete cavity

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obliteration, transabdominal ultrasound or laparoscopy may be used to help guide the procedure.

A central, as of yet unresolved, question is how to most effectively maintain cavity integrity after the surgical procedure. Most authorities agree that estrogen after the procedure to stimulate endometrial growth is important, however, little evidence exists to suggest the ideal dosing regimen or length of estrogen therapy (1, 4–6, 8, 9). Beyond the use of estrogen, little consensus exists on postoperative management. There are data that describe short-term placement of intrauterine objects such as balloons, catheters, or intrauterine devices (IUDs) (1, 4–6, 8), while other data suggest placing nothing in the uterine cavity postoperatively (9). During postoperative second-look office hysteroscopies, we noted a gradual progression of recurrent adhesions over time. Initial attempts to bluntly break the newly forming adhesions with the flexible hysteroscope were successful. This early experience evolved into our current approach for maintaining endometrial cavity patency postoperatively.

Our protocol requires patients to return for flexible office hysteroscopy within 2 weeks of the procedure to bluntly lyse newly forming filmy adhesions before these adhesions become dense and vascularized. Patients continue to return every 1–3 weeks to repeat the procedure until no further adhesion reformation occurs. Our data suggest that this typically requires two to three postoperative office procedures. This retrospective pilot study is the first description of this technique for the postoperative management of patients with Asherman's syndrome. It was performed to assess whether the technique is effective and warrants further study.

MATERIALS AND METHODS

From January 2003 through June 2005, 25 women completed hysteroscopic treatment of intrauterine adhesions by a single surgeon after presenting with complaints of menstrual abnormalities, dysmenorrhea, and/or infertility. Patients' ages ranged from 29 to 49 years. Demographic data were collected via a retrospective chart review, including patient age, pregnancy history, presenting symptoms, menstrual characteristics, antecedent procedures, and subsequent outcomes when available.

The diagnosis of intrauterine adhesions was confirmed by office hysteroscopy in all cases before scheduling operative treatment. Sharp hysteroscopic adhesiolysis under general anesthesia was performed to treat all patients using a 5.5-mm O.D. rigid hysteroscope system (Karl Storz Endoscopy, Culver City, CA) with continuous monitored saline flow and blunt tipped scissors. In cases with cavity obliteration, transabdominal ultrasound was used to help guide the procedure. After adhesiolysis, cervixes were dilated to 26 Fr. This treatment was followed by 25 days of oral conjugated estrogens (2.5 mg) and 5 days of combined conjugated estrogens/medroxyprogesterone acetate (2.5/10 mg) therapy. Serial postoperative office hysteroscopy using a 3.5-mm O.D. flexible hysteroscope (Karl Storz Endoscopy) was used to perform blunt adhesiolysis of newly forming recurrent synechiae.

No preprocedural medications, cervical blocks, or cervical instrumentation were ever used to perform the office-based procedures. No procedures exceeded 5 minutes, and all were well tolerated. No pre-, intra-, or postprocedural complications were encountered. Initial postoperative office hysteroscopies were performed within 2 weeks of the primary surgery. Subsequent office hysteroscopies were performed every 1–3 weeks until minimal to no disease remained or further improvement was deemed unlikely. After completion of therapy, clinical indicators such as menstrual pattern and fertility were used to assess whether further intervention was warranted. The mean and median number of follow-up office procedures was three.

After reviewing four previously published staging systems (4, 10–12) we decided to use a modified version of the staging system originally described by March et al. (10) (Table 1). This wholly anatomic staging system allowed us to perform serial staging before each procedure (operating room [OR] or office based) without regard to menstrual flow status.

Staging of disease at the time of the initial sharp adhesiolysis and all subsequent blunt adhesiolysis procedures were determined by reviewing dictated operative reports and videos recorded at the time of the procedures. These were reviewed by two different blinded observers and compared to ensure consistency in interpretation of the staging. In two cases, a third observer, the primary surgeon, was used

TABLE 1

March classification (1).

Minimal	Moderate	Severe
< 1/4 of uterine cavity involved; thin or filmy adhesions; ostial areas and upper fundus minimally involved or clear	1/4 to 3/4 of uterine cavity involved; no agglutination of walls; adhesions only; ostial areas and upper fundus only partially occluded	> 3/4 of uterine cavity involved; agglutination of walls or thick bands; ostial areas and upper cavity occluded

Note: In cases where cavity integrity has been restored but ostial occlusion still exists, a classification of moderate applies.

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to stage disease owing to a discrepancy of the staging between the blinded observers.

After obtaining protocol acceptance from our institutional review board for research involving human subjects, we attempted to contact all 25 patients by telephone to obtain informed verbal consent, verify case histories, and collect primary follow-up outcome data. Primary outcome data included current menstrual cycle pattern and flow, presence or absence of dysmenorrhea, and fertility outcomes. Participants' perceptions of the success of their treatment were also recorded.

Given the evolutionary development of this approach, pretreatment institutional review board approval was never sought. Patients were counseled that no definitive data existed to suggest the optimal postoperative approach to Asherman's syndrome. The primary surgeon's (KI) approach was clearly outlined, including his rationale and anecdotal experience. Other better described approaches to maintaining cavity patency were also presented. A single patient treated for Asherman's syndrome during the study period requested postoperative treatment with antibiotics and an intrauterine Foley balloon. Her request was honored, and her data are not included for the purposes of this study. Study exclusion criteria included patients opting for a different postoperative management approach, patients who did not follow-up for postoperative management, and patients who refused to be included in the study. All patients who met inclusion criteria, regardless of extent of disease or prior treatment failure, were included in the review.

Nonparametric ordinal menstrual flow and dysmenorrhea outcome data were compared with pretreatment values using the Wilcoxon signed ranks test at the 95% confidence interval level.

RESULTS

Twenty-five patients completed primary hysteroscopic adhesiolysis followed by serial office hysteroscopy between January 2003 and June 2005 for the treatment of Asherman's syndrome. Twenty-one patients consented to participate in the study and supplied primary follow-up outcome data. One patient was contacted and refused to allow us to use her medical information. Three patients were unreachable and therefore only secondary outcome (chart review) data are included for them. Thirteen of the 24 included patients have been followed for over a year since their last procedure, four patients for greater than 6 months, and seven patients for under 6 months.

Of the 24 included patients, 83% (20/24) initially presented with amenorrhea or oligomenorrhea, 67% (16/24) with infertility or recurrent miscarriage, and 54% (13/24) with dysmenorrhea. Most patients presented with more than one of these complaints. Twelve patients were initially diagnosed by hysterosalpingogram or sonohystogram; the remaining 12 were originally diagnosed hysteroscopically after failing to menstruate after P withdrawal. At initial surgical adhesiolysis, 50% (12/24) were diagnosed with

severe intrauterine adhesions, 46% (11/24) with moderate disease, and 4% (1/24) with minimal disease.

The most frequent causes of intrauterine adhesions were dilatation and evacuation (D&E) for a first trimester elective or missed abortion and uterine evacuation for postpartum hemorrhage in the second or third trimester. One of these events preceded adhesion formation in 79% (19/24) of patients. Postpartum instrumentation for hemorrhage including manual removal of the placenta accounted for 47% (9/19) of these patients, while first trimester procedures preceded adhesions in 42% (8/19) of this subset. The two remaining patients required repeat D&E after an original second trimester curettage. Of the eight first trimester D&Es, six required more than one procedure to completely evacuate the uterus and control bleeding. The five other causes of Asherman's syndrome included one prior hysteroscopic myomectomy, one open myomectomy, two primary cesarean sections (one resulting in endomyometritis), and one curettage for endometrial cells on a PAP smear (Table 2).

Among the 21 respondents, there was a statistically significant improvement in menstrual abnormalities over the treatment period. Ninety-five percent (18/19) of patients initially presenting with menstrual flow abnormalities (amenorrhea or oligomenorrhea) had resumption of normal menses after treatment ($P < .0001$). Relief of dysmenorrhea occurred in 92% (12/13) of responding patients ($P = .0002$).

Of the 15 patients initially presenting with fertility concerns, four have delivered viable infants and three are currently pregnant (two in the third trimester and one at 11 weeks' gestation). Three patients have conceived but

TABLE 2
Etiology of intrauterine adhesions.

Antecedent intrauterine trauma	Valle and Sciarra (4) (n = 187)	This study (n = 24)
Curettage	183 (97.9)	20 (83.3)
Incomplete abortion	92 (50.3)	8 (33.3)
Postpartum bleed	44 (24.0)	9 (37.5)
Elective abortion	32 (17.5)	2 (8.3)
First trimester	14	2
Second trimester	18	0
Missed abortion	11 (6.0)	1 (4.2)
Trophoblastic disease	2 (2.2)	1 (4.2)
Other curettage	0 (0)	1 (4.2)
Open myomectomy	2 (1.1)	1 (4.2)
Hysteroscopic myomectomy	0 (0)	1 (4.2)
Other hysteroscopy	0 (0)	1 (4.2)
Abdominal metroplasty	1 (0.5)	0 (0)
Endometritis	1 (0.5)	0 (0)

Note: Data are n (%).

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miscarried in the first trimester (two of them twice). One of these patients has a homozygous thrombophilia. Of the five remaining patients who have not conceived, two have diminished ovarian reserve, one never developed viable endometrium after surgery, and one has been attempting pregnancy for only 2 months. Of the seven patients who have delivered viable infants or are currently pregnant, four initially had severe disease and three had moderate disease.

After primary surgery and all follow-up office hysteroscopies, 92% (22/24) of patients demonstrated an overall improvement in the stage of their Asherman's syndrome (secondary outcome measure). At the conclusion of their treatment, 75% (18/24) of patients had minimal to no disease. In patients initially diagnosed with severe disease, 58% (6/12) had minimal to no disease at the end of their treatment. In patients initially diagnosed with moderate disease 91% (10/11) had minimal to no disease at the conclusion of their therapy. Table 3 summarizes the presenting symptoms, initial and preprocedural stages, number of postoperative procedures, and final outcomes for all included study subjects.

DISCUSSION

While general consensus exists on the necessity of hysteroscopic adhesiolysis followed by hormone therapy for the treatment of Asherman's syndrome, there are little comparative data to suggest the ideal dose or course of hormone therapy. We chose to use 2.5 mg of conjugated estrogens at 4 times the standard physiologic dose to stimulate rapid endometrial proliferation after primary surgery. While others have opted to use even higher doses, it is unclear from the literature that enough benefit exists to outweigh the increased side effect and risk profile. As our approach relies on serial hysteroscopy to assess and lyse newly forming adhesions, we limited the course of high-dose hormone therapy to 1 month to minimize the amount of time endometrial proliferation would adversely affect visualization of newly forming adhesions.

There are also little data to suggest the most efficacious postoperative approach for the maintenance of endometrial cavity patency. A single study comparing the postoperative use of an IUD versus a Foley catheter suggests some advantage to the catheter-based approach. In this study, Orhue et al. (5) compared outcomes between 51 patients treated with an IUD in one 4-year period with 59 patients treated with a Foley catheter in the subsequent 4 years. In their catheter group, 81% of patients had resumption of normal menses, compared with 63% in the IUD group. Our smaller cohort had a somewhat better rate of normal post-therapy menses (95%), but given the differences in regional and individual surgical approaches to the disease, no valuable conclusion can be reached. In Valle and Sciarra's cohort of 187 patients, most of whom received a postoperative IUD, 88% of patients had return of normal menstrual cycles (4). This is comparable to our data.

With respect to fertility, March's review of numerous studies places the postoperative pregnancy rate between

60% and 75% (1), although Valle and Sciarra report a rate of 93% in those with minimal disease (4). Pregnancy rates are encouraging, but the true measure of reproductive success is viable births. Valle and Sciarra report term pregnancy rates of 55.6% in patients initially presenting with severe adhesions and 87.5% in patients who initially had mild disease (4). Schenker's findings correlate well with Valle and Sciarra's findings. He notes a 95% pregnancy rate with a 15% abortion rate in patients who had mild adhesions and a 60% pregnancy rate with a 50% abortion rate in patients initially presenting with severe disease (6). In our smaller series, 10 of 15 fertility patients had severe disease initially. Of those, 70% (7/10) conceived and 40% (4/10) have either delivered or are well established in their pregnancies. In the five fertility patients who initially presented with mild to moderate intrauterine adhesions, 60% (3/5) of them conceived and none aborted. These data, while limited by small numbers, appear to compare favorably to other published reports.

Other researchers have confirmed etiologic factors originally described by Asherman, identifying both risk and prognostic factors. In 1993, using hysteroscopy, Friedler et al. found an incidence of 19% of intrauterine adhesions after missed abortion (13). In 1994, Römer found the incidence of adhesions to be 30% after dilatation and curettage for incomplete or missed abortion (14). In 1991, Lurie et al. found an incidence of up to 39% among women who underwent dilatation and curettage after induced midtrimester abortion (15). In 1998, Westendorp et al. performed a prospective study to assess the prevalence of intrauterine adhesions among 50 women undergoing secondary removal of placental remnants 24 hours after delivery or a repeat curettage for incomplete abortions. Hysteroscopy was performed 3 months after interventions. Up to 40% of women were found to have intrauterine adhesions; in 75% of these cases the adhesions were classified as moderated to severe. Menstrual disorders were correlated to a statistically significant 12-fold increased risk for Asherman's syndrome (16). Based on these studies, it is likely that the overall incidence of intrauterine adhesions is considerably higher than generally recognized by gynecologists.

Table 2 compares the etiology of Asherman's syndrome in our patient population with the 187 patients in Valle and Sciarra's series (4). Again, while our overall numbers are small, there is good correlation between most common etiologies in both groups.

It bears repeating that postoperative office hysteroscopy with a small-gauge flexible hysteroscope requires no more time than a routine postoperative check and has been universally well tolerated in our patient population without the use of medication or a tenaculum. By avoiding placement of intrauterine balloons, our patients do not require prophylactic antibiotic treatment, and the risk of an inflammatory response associated with placement of a foreign body in the uterus is presumably diminished. IUDs are routinely left in place for months, during which time patients have no idea whether

TABLE 3

Presentation, Staging, and Outcome.

Patient	Presentation symptoms	Initial stage	Office hysteroscopy stage									Outcome			
			I	II	III	IV	V	VI	VII	VIII	IX	Menses	Dys	Pregnancy	
1	Dys, Inf	Sev	Mod										Light	No	No, IUI × 1
2	Amen, Dys, Inf	Sev	Min										Light	No	Yes, current term preg
3	Amen, Dys	Mod	Min	Min	Nml								Light	No	
4	Amen, Dys, Inf	Mod	Min	Min	Nml	Nml							Light	No	Yes, term delivery
5 ^a	Inf	Min	Nml										Uncontacted		
6	Amen	Mod	Mod	Mod									? Preg		
7	Amen, Dys, Inf	Sev	Mod	Mod	Mod								Light	No	Yes, Mab × 2
8	Oligo	Sev	Min	Min	Min	Min							Mod		
9 ^a	Amen	Mod	Min										Uncontacted		
10	Amen, Inf	Sev	Min	Min									Light		Yes, current term preg
11	Amen, Inf	Sev	Mod	Mod	Min	Mod OR	Mod	Mod					Amen		No, IVF/Amen
12	Amen	Mod	Min	Nml									Light		
13	Amen, Dys, Inf	Mod	Min	Min									Heavy	No	Yes, term delivery
14	Amen, Dys, Inf	Mod	Min	Nml									Mod	No	Yes, current 11 week gestation
15	Oligo, Dys, Inf	Sev	Min										Mod	Mod	Yes, term delivery
16	Amen, Dys, Inf	Sev	Mod										Light	No	Yes, SpAb × 2
17	Amen, Dys, Inf	Sev	Mod	Mod	Sev Mab D&C	Mod	Sev OR	Min	Mod	Mod, OR	Min, PPROM, D&E		Mod	Min	Yes, current, preterm preg
18	Amen, Dys, Inf	Sev	Mod	Mod	Sev OR	Mod	Mod	Sev	Mod	Sev			Mod	No	No, endometrium never seen
19	RAb	Sev	Min	Min											Yes, SpAb
20	Oligo, Inf	Mod	Min										Mod		No, not trying yet
21 ^a	RAb	Mod	Min	Min									Uncontacted		
22	Amen, Dys	Sev	Min	Min	Nml								Light	No	
23	Amen	Mod	Min	Nml									Mod		
24	Amen, Dys	Mod	Min	Nml									Heavy	No	

Note: Amen: amenorrhea; D&C: dilatation and curettage; D&E: dilatation and evacuation; Dys: dysmenorrhea; Inf: infertility; IUI: intrauterine insemination; Mab: missed abortion; Min: minimal; Mod: moderate; Nml: normal; Oligo: oligomenorrhea; OR: returned to operating room; PPRM: premature preterm rupture of membranes; Preg: pregnancy; Rab: recurrent abortion; Sev: severe; SpAb: spontaneous abortion.

^a Patients unreachable. No primary outcome data available.

their treatment will be successful or not. This approach has the potential dual benefit of providing early and ongoing feedback to patients on their progress and decreasing the time interval between primary hysteroscopic surgery and resumption of normal function.

While our findings are encouraging, the true value of this novel approach warrants further study. To prove that second- and third-look office hysteroscopic adhesiolysis is superior to the balloon or IUD for preventing recurrent intrauterine adhesions, a well designed prospective, randomized, multicentered trial to evaluate the different postoperative approaches to the management of Asherman's syndrome is necessary.

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