Arch Gynecol Obstet (2016) 294:411–416
DOI 10.1007/s00404-016-4107-9

Hysteroscopic adhesiolysis: efficacy and safety

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Received: 27 November 2015 / Accepted: 22 April 2016 / Published online: 29 April 2016

Abstract
Objective To evaluate the efficacy and safety of hysteroscopic adhesiolysis in patients with intrauterine adhesions (IUAs).
Setting Minia Maternity University Hospital, Egypt.
Design Prospective cohort study.
Patients This study included 61 patients presented with infertility (primary or secondary) or recurrent pregnancy losses caused by IUAs.
Intervention(s) The adhesions were divided by semi-rigid scissors introduced under direct vision through hysteroscopy. Three months later, second-look hysteroscopy was performed.
Primary outcome parameters Primary outcome parameters were reproductive parameters (pregnancy rate, duration of pregnancies, life births rate, time lag between the intervention and diagnosis of pregnancy).
Secondary outcome parameters Secondary outcome parameters were the changes in post-operative menstrual pattern, number and duration of intervention and type of intra- and post-operative complications.
Result(s) Pregnancy rate changed from 18 to 65.5 %, while live birth rate improved from 14.7 to 36 %. The mean time until the first conception was 10.2 months (range 2–60 months) after the operation. There was significant negative correlation between the degree of IUAs and the improvement in reproductive performance. Hysteroscopic adhesiolysis significantly improved menstrual pattern in 60.7 % of patients complaining of hypomenorrhea or amenorrhea. ($p = 0.0017$). The average operative time was 29 ± 10.2 (10–52) min and the hospital stay was 12.5 ± 2.1 (9–24) h. Uterine perforation occurred on 3 (4.9 %), and cervical laceration occurred in one case (1.6 %).
Conclusion(s) Hysteroscopic adhesiolysis of IUAs is safe and effective in terms of reproductive outcome. The outcome is significantly affected by degree of intrauterine adhesions rather than the main complaint before the procedure.

Keywords Hysteroscopic adhesiolysis · Intrauterine adhesions · Reproductive outcome

Introduction

Intrauterine adhesions (IUAs), also known as Asherman syndrome result after trauma to the basal layer of the endometrium. This may occur as a complication of pregnancy-related curettage. Also injury to the endometrium of a non-gravid uterus, including dilatation and curettage for diagnostic purposes, myomectomy, and hysteroscopic surgery, can also lead to IUAs [1].

Symptoms of intrauterine adhesions vary from no symptoms to menstrual complaints like hypomenorrhea or amenorrhea. Intrauterine adhesions may present with reproductive failure, as infertility and recurrent pregnancy loss [2].

Women with severe Asherman syndrome may require more than one imaging modality to establish the extent of

Registration Number: The trial was registered in the Australian and New Zealand Clinical trial registry under number: ACTRN12615000899549.

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disease and determine the prognosis for repair, and more than one approach to minimize recurrence of adhesions. Preoperative assessment of Asherman syndrome may include hysterosalpingography (HSG), hysteroscopy, transvaginal ultrasonography, or saline infusion sonohysterography [3]. Many preoperative, intraoperative, and post-operative measures have been described to improve surgical outcomes, including hormonal manipulation with estrogen (E) to induce endometrial proliferation, ultrasound-directed hysteroscopic lysis of synechia, and mechanical separation of the endometrium [4].

Nowadays, hysteroscopy is the method of choice to diagnose, treat, and follow-up patients with intrauterine adhesions [5].

This study aimed to assess the efficacy and safety of hysteroscopic adhesiolysis in patients with Asherman's syndrome by measuring the clinical pregnancy rate and live birth rate, resumption of menses, and intraoperative and post-operative complications.

Patients and methods

This prospective study was conducted at Minia University Maternity Hospital, Faculty of medicine Minia University, between January 2008 and October 2013. The study was approved by scientific ethical committee of the department of Obstetrics and Gynecology, on October 2008, and the Institutional Review Board of the University Hospital-Quality control unit of the Faculty of Medicine, Minia University on December 2008.

The study included 61 patients with reproductive failure (primary infertility, secondary infertility, recurrent pregnancy losses and/or preterm deliveries) due to intrauterine adhesions. Primary infertility was defined as failure of conception after 12 months of regular marital life. Secondary infertility was defined as the inability to conceive after 12 months without contraception in spite of regular marital life after having already conceived at least once. Recurrent pregnancy loss was defined as three or more successive spontaneous pregnancy losses before 13 weeks gestation (recurrent first trimester miscarriage) or between 13 and 24 weeks (recurrent second trimester miscarriage). Preterm delivery was defined as spontaneous onset of labor between 24 and 37 weeks. The study included patients attending our tertiary referral hospital complaining of reproductive failure (primary infertility, secondary infertility, recurrent pregnancy losses) and they were diagnosed to be due to IUAs.

Patients with the following inclusion criteria were invited to participate in the study: patients with intrauterine adhesions that affect their reproductive carrier, with no contraindication for either pregnancy or surgery. Patients with the following criteria were excluded from the study: age >37 years old, other causes of amenorrhea or reproductive failure as ovulatory disorder, tubal block, pelvic adhesions diagnosed by laparoscopy, PID or male factor.

The study aim and procedure were explained to all patients and written informed consents were taken from all patients prior to enrollment.

All of the patients and their partners underwent thorough history taking, systematic clinical examination and local pelvic examination, routine laboratory investigations as CBC, liver and kidney functions to exclude general disease contraindicating pregnancy or surgery. All of the patients, and their partners had complete infertility investigations, including sexually transmitted disease work-up, semen analysis, endocrine evaluation as necessary, assessment of ovulation by day three FSH and E2 test results, also recurrent miscarriage work-up.

The work-up to document the degree of intrauterine synechia included hysterosalpingography, pelvic ultrasound (using 7.5 MHz intracavitary probe, Sonoace 9900, Medison, Seoul, Korea) and office hysteroscopy (Versascope of Gyncare, USA) with diameter of 2.9 mm. Diagnostic laparoscopy was done as a part of routine infertility work-up.

Patients were stratified according to the degree of intrauterine adhesions according to the American fertility Society classification of intrauterine adhesions 1988 and each block was further subdivided into three blocks according to the main complaint (primary, secondary infertility and recurrent pregnancy loss).

Outcome measures

Primary outcome parameter was reproductive parameter (pregnancy rate, duration of pregnancies, life births rate and time lag between the intervention and diagnosis of pregnancy). The secondary outcome parameters were the changes in post-operative menstrual pattern, number and duration of intervention and type of intra- and post-operative complications to gain information on the safety of the procedure.

Procedures

All procedures were performed as in-patient procedures during the follicular phase of the menstrual cycle. We used intra-vaginal misoprostol 400 mcg for cervical ripening. All hysteroscopic procedures were performed under general anesthesia. All the procedures were done under trans abdominal ultrasound guidance to identify the uterine cavity especially in patients with severe adhesions.

The cervix was dilated to Hegar dilator 6. A forward oblique 30°, hysteroscopy was inserted inside the uterine

cavity that was distended with 0.9 % normal saline at inflow pressure of 60–90 mmHg, using a special machine, hysterometer, which was used to adjust the pressure of the flow, the amount of the distension media fluid used and the deficit after the operation.

The operative hysteroscopy used was 5.5 mm outer sheath diameter that permits the use of 3–5 French diameter semi-rigid scissors to lyse the adhesion at the junction of the adhesion with the endometrium and excise the tissue.

The operative time was recorded for each patient. All intra or post-operative complications as hemorrhage, perforation or incomplete adhesiolysis were recorded. Data on the subsequent reproductive performance of each patient were recorded.

Pediatric Foley's catheter No 10 F was inserted using a straight artery forceps for 10 days after lysis of adhesions for prevention of re-adhesions. The balloon was inflated with 3 ml of normal saline. Cyclic estrogen (estradiol valerate 2 mg/day for 21 days) and progestogens (norgestrel 0.5 mg/day in the last 10 days of the estrogen treatment) for 3 months were prescribed for all women.

Follow-up

All patients were instructed about the expected post-operative complications and were asked to report any abnormal complaints.

Three months later, second-look hysteroscopy has been performed after completion of the cyclic hormonal treatment to diagnose the degree of adhesiolysis and formation of re-adhesions.

Hysteroscopically guided adhesiolysis for patients with Asherman's syndrome: menstrual and fertility outcomes data were statistically described in terms of range, mean ± standard deviation (±SD), median, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables between different groups in the present study was done using Mann–Whitney *U* test for independent samples. For comparing categorical data, Chi-square test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity and specificity.

Correlation between various variables were done using Pearson moment correlation and Spearman rank correlation equations. A probability values (*p* value) less than 0.05 were considered statistically significant.

All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA), SPSS (Statistical Package for the Social Science; SPSS; Inc., Chicago, IL, USA version 20) and Arcus Quick Stat (Biomedical version, Addison Wesley Longman Ltd, USA) statistical program.

Results

A total of 72 women were enrolled in the study. Intrauterine adhesions were related to curettage for pregnancy complications, such as missed or incomplete miscarriage in 35 cases, in 11 cases intrauterine adhesions were caused by curettage following postpartum hemorrhage, or retained placental remnants., Intrauterine adhesions were diagnosed following cesarean sections in 9 cases, as a sequelae of PID in 9 cases, 4 cases following hysteroscopic surgery, one case following HSG and 3 cases caused by TB endometritis. Only 61 patients completed the follow-up protocol and were available for statistical analysis. The demographic characteristics of the patients are shown in Table 1.

Fifteen (24.6 %) patients had primary infertility. There were 35 cases of secondary infertility 9 cases following term vaginal deliveries and 26 case following miscarriages. The eleven cases with recurrent pregnancy loss were distributed as follow 4 (6.5 %) patients had recurrent first trimester miscarriage, 5 (8.2 %) patients had recurrent second trimester miscarriage, and 2 (3.3 %) patients had preterm delivery (Table 2).

The operation was done successfully for 42/61 (68.9 %) cases, 13 (21.3 %) cases required second intervention. In the remaining 6 (9.8 %) cases; the cycle of operative hysteroscopy and the 3 months interval second-look hysteroscopy was repeated and the final decision was failure of the procedure to treat intrauterine adhesions in these 6 cases.

The operative time ranged between 10 and 52 min (29 ± 10.2), hospital stay ranged between 9 and 24 h (12.5 ± 2.1). Operative complications as shown in Table 3 were minimal Accidental perforation was noted in three cases. Reformation of adhesion after complete adhesiolysis

Table 1 Demographic characteristics of patients

Demographic characteristics	Range (mean ± SD)
Age (years)	20–35 (27.3 ± 4.8)
Gravidity	0–6 (1.9 ± 1.5)
Duration of follow-up (months)	1–60 (33.5 ± 10.7)

Table 2 Distribution of the patients according to the clinical finding

	Mild	Moderate	Severe	Total
Primary infertility	2	5	8	15
Secondary infertility	14	18	3	35
RPL	8	3	0	11
Total	24	26	11	61

was noted in one case. Post-operative complications did not require extra hospitalization.

In the current study, hysteroscopic adhesiolysis significantly improved menstrual pattern in 60.7 % of patients. ($p = 0.0017$).

The mean time until the first conception was 10.2 months (range 2–26 months) after the operation. Nine women got pregnant twice during the study period. There was statistically significant improvement in the reproductive outcome after the procedure ($p = 0.0001$). There was statistically significant difference in the pregnancy rate, live birth rate and gestational age before and after the procedure ($p = 0.0001$, 0.0118, 0.001, respectively) (Tables 4, 5, 6, and 7)

Table 3 Operative and post-operative complications of hysteroscopic adhesiolysis

Complications	Number and %
Cervical laceration	1 (1.6 %)
Uterine perforation	3 (4.9 %)
Fluid overload	0
Blood loss	
Mild	54 (88.5 %)
Moderate	7 (11.5 %)
Severe	0
Post-operative pain	
None	47 (77 %)
Mild	
Severe	14 (23 %)0
Post-operative fever	4 (6.5 %)
Intrauterine adhesions	1 (1.6 %)
Paralytic ileus	1 (1.6 %)

Table 6 Obstetric outcome classified by the degree of IUA

	Mild	Moderate	Severe	Total
No Pregnancy	4	8	9	21
1st trimester abortion	1	5	0	5
2nd trimester abortion	5	4	0	9
PTL	3	2	1	6
FTP	11	7	1	19
Total	24	26	11	61

PTL preterm labor, *FTP* full term pregnancy

Discussion

During the last two decades, diagnosis and treatment of intrauterine adhesions progressed dramatically by the widespread use of hysteroscopic surgery [6].

Various hysteroscopic adhesiolysis techniques were described and published in the last decades, either division of adhesion by hysteroscopic scissors [7] or by using the resectoscope [8].

The exact prevalence of the condition is difficult to determine, but the incidence has been increasing over the last few decades, probably due to increase in iatrogenic endometrial trauma as well as due to better diagnostic techniques like transvaginal ultrasound and hysteroscopy [9]. Typical presentations of Asherman's syndrome are amenorrhea, hypomenorrhea, infertility and repeated abortions [10].

There are no high quality data regarding the efficacy of methods to prevent post-operative adhesions. Two small studies that evaluated women after adhesiolysis with no post-operative treatment reported inconsistent results. Some women underwent two to three procedures, and the

Table 4 Menstrual pattern before and after the procedure

	Normal Menses	Hypomenorrhea	Amenorrhea	*p* value
Before: no (%)	33 (54.1)	17 (27.9)	11 (18)	0.0017
After: no (%)	50 (81.9)	5 (8.2)	6 (10)	

Table 5 Obstetric outcome classified according to the clinical presentation

	Primary infertility ($n = 15$)			Secondary infertility ($n = 35$)			RPL ($n = 11$)			Total
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe	
No Pregnancy	0	1	6	4	7	3	0	0	0	21
1st trimester abortion	0	1	0	1	2	0	0	2	0	6
2nd trimester abortion	1	0	0	3	3	0	1	1	0	9
PTL	0	0	1	1	2	0	2	0	0	6
FTP	1	3	1	5	4	0	5	0	0	19

PTL preterm labor, *FTP* full term pregnancy

Table 7 Obstetric outcome before and after hysteroscopic adhesiolysis

Variable	Before adhesiolysis	After adhesiolysis	*p* value
Clinical pregnancy rate (*N*, %)	11/61 (18 %)	40/61 (65.5 %)	0.0001
Live birth rate (*N*, %)	9/61 (14.7 %)	22/61 (36 %)	0.0118
Gestational age in weeks (range, mean ± SD)	0–40 (23.3 ± 15.2)	0–40 (29.3 ± 15.4)	0.0323

post-operative pregnancy rate was 42 of 47 women in one study, but only 9 of 24 in the other [11].

The insertion of intrauterine device (IUD) or Foley's catheter balloon has been advocated by various authors as an effective and widely used method to prevent adhesion reformation [4].

We, therefore, in the present study used Foley's catheter with inflated balloon for few days after lysis of adhesions for prevention of re-adhesions. Simultaneously, we also started cyclic estradiol valerate 2 mg/day for 21 days and norgestrel 0.5 mg/day in the last 10 days of the estrogen treatment for 3 months. One study ($n = 110$) compared outcomes for a bladder catheter or IUD, and found that the bladder catheter resulted in a greater proportion of women achieving normal menses (81 versus 63 %), higher conception rates (34 versus 23 %), and a reduced need for reoperation [4].

There are few data to compare use of estrogen with other interventions. The only comparative study ($n = 35$) found no difference in pregnancy rate in women treated with estrogen therapy alone compared with estrogen in combination with an IUD [12].

The mean duration of the hysteroscopic adhesiolysis procedure had ranged between 10 and 52 min.

There are several reasons that make comparison of different results complex. First, there are different classification systems and the management plans applied depend to a large extent on the classification used [13]. Second, the outcome of treatment are not displayed according to the presenting symptoms [7, 14]. Some women with Asherman's syndrome present with hypo- or amenorrhea, some with infertility, and others with recurrent pregnancy loss. It is quite possible that the presenting symptom may affect the outcome. Third, the reproductive outcomes in many previous reports were simply presented as rough pregnancy rate without reference to the cumulative pregnancy rate and the duration of follow-up, which is a much more accurate method of providing data on pregnancy after treatment [15, 16].

It has been reported that the return of menstruation after hysteroscopic treatment ranges from 52.4 to 88.2 % [2, 10]. In a systematic review of 28 studies, most studies reported that approximately 80–100 % of women had an improvement in menstrual flow. In the present study, the improvement of menstrual pattern was 60.7 % (17 out of 28), which was similar to earlier reports.

In a systematic review of 28 studies, most studies reported a pregnancy rate of 40–80 % and a live birth rate of 30–70 % [17]. In the present study, clinical pregnancy rate before hysteroscopic adhesiolysis was 11/61 (18 %) and was 40/61 (65.5 %) after the procedure (p value = 0.0001). Live birth rate was 9/61 (14.7 %) before the procedure and 22/61 (36 %) after the procedure (p value = 0.0118).

The overall gestational age in weeks was 23.3 ± 15.2 before the procedure and was 29.3 ± 15.4 (p value = 0.0323).

The data regarding treatment outcomes for intrauterine adhesions are from small observational studies. The study design and results are inconsistent, and high quality data are needed. A recent Cochrane review concluded that more randomized studies are needed to substantiate the effectiveness of the hysteroscopic removal of suspected endometrial polyps, submucous fibroids, uterine septum or intrauterine adhesions in women with unexplained subfertility or prior to IUI, IVF or ICSI [18].

Acknowledgments The current study was done and funded by Minia Maternity University Hospital as Scientific Research Plan.

Compliance with ethical standards

Conflict of interest Both Authors declare that they have no conflict of interest.

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