

Hysteroscopic treatment of Asherman's Syndrome

Asherman Sendromu'nun Histeroskopik Tedavisi

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SUMMARY






Objective: To assess the achievement of hysteroscopic treatment for Asherman's Syndrome(AS), also called 'intrauterine adhesions(IUAs) or Intrauterine synechiae'.

Method: Retrospectively, 27 patients with AS were enrolled in our study at Ankara liv hospital between 2017-2019. These patients were evaluated with hysteroscopically then they had adhesiolysis at the same session. The monopolar knife was used for adhesiolysis and the operation was gone on until adequate cavity enlargement was achieved. Intrauterine device (IUD) was placed in the new occurred cavity, and combined hormonal therapy(high dose estrogen and progesterone) was given for two months. American Fertility Society classification was used for scoring of IUAs. After IUD was taken out, they were called, and their menstrual pattern and fertility status were learned. If their symptoms recurred they were hysteroscopically evaluated again.

Results: 27 patients were hysteroscopically diagnosed as AS. 15 of them had reproductive problems, and other 12 patients had an only menstrual abnormality. Thirteen patients had pregnancy-related curettage; four patients had dilatation and curettage(D&C) for their menstrual problems. After hysteroscopic treatment, 6 of 12 patients with only menstrual abnormality had a normal menstrual pattern, 2 of them did not have a normal period but a little bit better(from amenorrhoea to hypomenorrhea). 8 of 15 infertile patients had positive pregnancy test(live born:6, spontaneous abortion:2). And also, all these pregnant women were second order infertile patients.

Conclusions: Hysteroscopy is the most useful technique for diagnosis and treatment for Asherman's Syndrome. And also, the hysteroscopic procedure has a positive effect on pregnancy rate and menstrual regularity.

Keywords: Asherman's Syndrome, intrauterine adhesions, hysteroscopic treatment

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ÖZET

Amaç: “İntrauterin adezyon (IUA)” veya “Intrauterin sineşi ”olarak da adlandırılan Asherman Sendromu (AS) için histeroskopik tedavinin başarısını değerlendirmek.

Yöntem: 2017-2019 yılları arasında Ankara Liv Hospital'deki AS'li 27 hasta retrospektif olarak değerlendirildi. Hastalara histeroskopi sonrası aynı seansta monopolar sistem ile adezyoliz uygulandı. Yeterli kavite sağlandıktan sonra yeni oluşan kaviteye intrauterin cihaz (RIA) yerleştirildi ve iki ay boyunca kombine hormonal tedavi (yüksek doz östrojen ve progesteron) verildi. IUA'ların derecelendirilmesi için American Fertility Society sınıflandırması kullanıldı. RIA çıkarılması sonrası hastalar tekrar değerlendirilerek adet düzenleri ve doğurganlık durumları öğrenildi. Eğer semptomları tekrarladıysa, tekrar histeroskopi uygulandı.

Bulgular: Histeroskopik olarak AS tanısı alan 27 hastadan 15 tanesinde üreme sorunu, diğer 12'sinde sadece menstrüel anomali vardı. Histeroskopik tedavi sonrası, sadece menstrüel anormalliği olan 12 hastanın 6'sında normal adet, ikisinde de normal olmasa bile iyiye gidiş (amenore'den hipomenore) izlendi. Tedavi sonrası infertil hastaların 8'inde gebelik elde edildi (canlı doğum: 6, spontan abort: 2). Gebelik elde edilen tüm hastalar sekonder infertil gruptaydı.

Sonuç: Histeroskopi, Asherman Sendromu tanı ve tedavisi için en faydalı tekniktir. Ayrıca, histeroskopik prosedürün hamilelik oranları ve adet düzeni üzerine olumlu etkileri vardır.

Anahtar sözcükler: Asherman Sendromu, intrauterin adezyon, histeroskopik tedavi

INTRODUCTION

Intrauterine adhesions are first reported in 1894 by Heinrich Fritsch¹ and further described by Asherman in 1948²⁻³. In these articles, the disease is described as a primary uterine disease, often presenting secondary amenorrhea because of trauma to the recently pregnant uterus, especially after D&C. By the time etiology, symptomatology, pathology, and treatment of AS are evolved. Currently, AS is defined as ‘partial or complete obliteration of the uterine cavity by adhesions with resulting menstrual abnormalities, infertility, or recurrent pregnancy loss.’ Although most cases are associated with trauma to basalis layer of endometrium from surgical procedures such as C&S, myomectomy, hysterotomy, D&C, manual removal of the placenta, non traumatic factors can be also related with AS like postabortal endometritis⁴, puerperal sepsis⁵, particular infections such as tuberculosis endometritis, caustic abortifacients and even normal delivery⁶. Postpartum curettage is the most devastating one.

Hooker et al. reported that the incidence of intrauterine adhesions after one D&C was found 16% and most of them were in the mild stage. After two and three procedures, the incidences were 14% and 32% respectively⁷. When the carriage is done during 2nd, 3rd, 4th postpartum week, risk of IUA gets higher. The endometrium may be more susceptible to trauma, especially the basalis layer in this period. Regardless of whatever reason, the prognosis of AS is poor. The symptomology is also now known to range from normal menstruation, through hypomenorrhea, to amenorrhea⁸, infertility and obstetrics

complications⁹. Patients with amenorrhea and cyclic pain can be associated with hematometria. In the presence of adhesions incidence of pregnancy-related abnormalities are higher than normal, like ectopic pregnancy, recurrent miscarriage, premature labor, and abnormal placentation⁸.

Pathology shows fibrous connective tissue with or without glandular tissue; this can be ranged from firm to dense. Treatment is always surgical and aims to restore the uterine cavity and prevent recurrent adhesions. Hysteroscopic lysis of adhesions is the main method of treatment of AS. Other treatments must be performed after hysteroscopy has failed. Most authors use an intrauterine device and high dose combined hormonal treatment (estrogen and progesterone) after hysteroscopic adhesiolysis. Treatment's outcomes are difficult to evaluate as there are no universally agreed on the classification system of AS. There is two familiar classification system for AS; American Fertility Society's (AFS) classification (Table 1) and European classification. AFS also includes the menstrual pattern. AS can cause abnormal placental implantation and subsequent blood loss, transfusion, and hysterectomy. The complications of the hysteroscopic procedure are, like other many surgical procedures, infection, bleeding, and uterine perforation. We reported our experience in the use of operative hysteroscopy at our hospital. This study aims to retrospectively evaluate the safety and efficacy of hysteroscopic adhesiolysis by observing re-establishment of the uterine cavity, postoperative resumption of menses, pregnancy rate, and outcomes.

Table 1: Intrauterine Adhesions Classification/American Fertility Society, 1998.

The extent of Cavity involved	<1/3	1/3-2/3	>2/3
Score	1	2	4
Type of Adhesions	Firmly	Firmly&Dense	Dense
Score	1	2	4
Menstrual Pattern	Normal	Hypomenore	Amenore
Score	1	2	4
Stage 1	Mild	1-4	
Stage 2	Moderate	5-8	
Stage 3	Severe	9-12	

MATERIAL AND METHODS

In Ankara liv hospital between 2017-2019, 27 patients were diagnosed with AS via hysterosalpingography(HSG). Demographic data were collected via a retrospective chart review, including patient age, pregnancy history, presenting symptoms, menstrual characteristics, past procedures, and subsequent outcomes when available.

Under general anesthesia and sterile conditions, all cases were hysteroscopically scored according to AFS Classification. (Table 1). The procedure was done in the early proliferative phase of the menstrual cycle in the patients who were menstruating. Prophylactic antibiotics cefamezine at the dose of 2 gr intravenous, were given routinely at the induction of anesthesia. 10mm rigid hysteroscope equipped with a hysteroscopic monopolar hook knife used for electrodissection was introduced into the cavity, obtained after prudent cervical dilatation by the Hegar's dilators. Glycine was used as a distending medium. The procedure was stopped after adhesiolysis, and enough uterine cavity was achieved.

Simultaneously diagnostic laparoscopy was performed for patients who were infertile to detect

if any other factor exists contribution to infertility. IUD (multi-load copper T) was inserted into the uterine cavity, and high dose combined hormonal therapy (estrogen and progesterone) was given to all patients for two months. At the end of the two months after IUD were taken out, the patients who had still menstrual abnormalities were evaluated again via outpatient hysteroscopy without anesthesia. Subsequent fertility was learned by calling all patients by the phone. The follow-up was defined as immediately after treatment for women who were trying for pregnancy.

RESULTS

Twenty-seven patients were hysteroscopically diagnosed as AS. The median age was 31 years (range 21-39).

15 of them had reproductive problems, and other 12 patients had only menstrual abnormality (Table 2). Twelve patients had only menstrual abnormalities. Eight of them had amenorrhea, four of them had hypomenorrhea. Fifteen patients had reproductive problems. Six of them were primer infertile, nine of them were seconder infertile. Three patients of secondary infertile had habitual abortus.

Table 2: Characteristics and post-treatment status according to clinical presentations

Clinic Presentation	Duration Mean (min-max)	Subclinical Form	Clinic after hysteroscopic treatment
Menstrual abnormality (n=12)	1,65years (4months-5years)	Amenorrhea (n=8)	6 patients: normal menstruation, 2 patients: a little bit better
		Hypomenorrhea (n=4)	No change
Reproductive problems (n=15)	6,2 years (1-17 years)	primer infertile (n=6)	No pregnancy
		seconder infertile (n=9)	No pregnancy
			8 pregnancy
			No pregnancy

In the obstetric histories; 48% (n: 13) patients had endometrial trauma on the gravid uterus. 15% (n: 4) patients had elective D&C, 37% (n: 10) had pregnancy-related curettage (incomplete abortion and intrauterine exitus at first trimester). Four patients out of 10 had D&C after postpartum placental retention. One patient had three times

D&C because of molar pregnancy. One patient underwent C&S after uterine rupture. One patient had hysterotomy due to intrauterine exitus of 18 weeks gestational age. Only one patient had D&C for menometrorrhagia, two patients had only C&S. (Table 3)

Table 3: Characteristics of AS patients undergoing hysteroscopy and number of cases due to Obstetric histories

Age Mean (min-max)	31 years (21-39)		
Stage of AS according to AFS classification at initial surgical adhesiolysis	Mild (n=6, 22%)		
	Moderate (n=13, 48%)		
	Severe (n=8, 30%)		
Obstetric histories (n=27)	Endometrial trauma on the gravid uterus (n=13)		
	Elective D&C (n=4)		
	Pregnancy related curettage (n=10)	D&C after postpartum placental retention (n=4)	
		Three times D&C because of molar pregnancy (n=1)	
		Underwent C&S after uterine rupture (n=1)	
		Hysterotomy due to intrauterine exitus of 18 weeks gestational age (n=1)	
		D&C for menometrorrhagia (n=1)	
Only C&S. (n=1)			

Mean infertility duration was 6,2years (1-17 years) and mean duration of menstrual problems was 1,65 years(4 months-5 years). The delay between the causal procedure and hysteroscopic treatment of IUA was unfortunately not available.

At initial surgical adhesiolysis, 22% (6/27) were diagnosed with mild stage, 48% (13/27) with moderate stage and 30% (8/27) with severe stage according to AFS classification of AS.

After hysteroscopic treatment, 6 of 12 patients with only menstrual abnormality had a normal menstrual pattern, 2 of them did not have a normal period but a little bit better(from amenorrhoea to hypomenorrhoea). Totally, 67%(8/12) patients

were satisfied with the treatment, all of these eight patients from the amenorrhic group.

After treatment, Only eight patients out of 15 (53%) were pregnant, and all of them were secondary infertile patients. Among eight patients, six of them were delivered with live-born children. One of them was preterm delivery, And two patients had a spontaneous abortion. We observed no ectopic pregnancy. There was no any placental implantation anomaly in our series.

A complication was noted only two patients out of 27 (7%) involving a perforation. One of them occurred during cervical dilatation, and another one was occurred during the hysteroscopy procedure, from the uterine fundus. The procedure

was stopped, and immediately defects were repaired via laparoscopy. No other complication was noted in our series. At the end of the two months after IUD were taken out, the patients who had still menstrual abnormalities were evaluated again via outpatient hysteroscopy without anesthesia. So four patients had two hysteroscopic sessions, and also one patient had three sessions.

DISCUSSION

Intrauterine adhesions, AS is one of the popular challenges for gynecologists. It can be confronted with very different and complicated clinical presentations; menstrual abnormalities, infertility, pregnancy complications, cyclic abdominal pain. However, we can classify these different symptoms into two categories: reproductive problems and menstrual disorders. The major risk factor for the AS is uterine trauma, especially associated with the post-pregnancy state, possibly related to hormonal changes at that time.

The treatment of uterine synechiae has largely benefited from technological progress in endoscopic surgery. Operative hysteroscopy must now be first performed in all cases of intrauterine adhesions. Scissors are the best instrument when the passage of the hysteroscope alone is insufficient. This method allows the use of a smaller operative sheath, which is important in cases where even dilating the cervix, can result in a false passage. Nd-YAG laser or electrosurgical energy could also be used, but these modalities pose a risk of endometrial destruction which would seem undesirable. Even though post-treatment adhesions may be unlikely most authors use adjunctive therapy. One of the most used modalities is hormonal therapy and IUDs. When estrogen encourages endometrial growth, IUD could prevent reformation of adhesions and, hopefully, on removal result in the breakdown of any new adhesions that had formed. The dangers of the device are minimal as infection probably occurs at the time of insertion if it does occur or as a result of sexually transmitted disease.

Treatments outcomes are difficult to assess as there are no universally agreed upon classification system. However, intrauterine pregnancies rate ranges from 22 to 45% and live births range from 28 to 32%. The risk of complications for those that achieve pregnancy is significant with a significant risk for placenta accrete and subsequent blood loss, transfusion, and hysterectomy.

Complications from pregnancy-related curettage are the most common cause of intrauterine

adhesions. In our series, 37% of the cases had a history for pregnancy-related curettage. In a series of 1858 cases, Schenker finds a history of trauma on a gravid uterus in 90.8%⁸; A study finds 30% of synechiae after requested legal abortions¹⁰. Hooker published a systematic review⁷: Hysteroscopy was performed at 4-6 weeks after curettage for first trimester abortion in 147 patients; in 28 patients (19%), one or more synechiae were found, the incidence of adhesions following only one abortion was 16,3%, 14% after two abortions and 32% after three or more abortions⁷. Cesarean section is exceptionally involved: 2,8% for Rochet¹¹ and 2% for Schenker⁸. Postpartum curettage is especially dangerous. According to Butram¹² and Parent¹³, post-partum curettage is traumatizing between the 1st and 4th week following delivery. The risk of adhesion is evaluated at approximately 25%^{11, 13}. Synechiae may be the cause of infertility; in fact, it is often associated with other genital lesions such as a tubal pathology, uterine malformation or sperm abnormality in a partner. In our series, the most confounding factor was tubal pathology. Consequently, a genital check-up of the infertile couple is necessary before starting a therapeutic procedure. Abnormal placentation is exceptional; Although Schenker finds two placentas previa (0,1%) and 22 accurate (1%) out of 2151 cases⁸, we have no any abnormal placentation in our series.

In our series, we note no infection or hemorrhage, but two uterine perforations occurred and were immediately diagnosed and repaired in the operation room at the same session. In case of severe adhesions, we performed an abdominal ultrasound control during hysteroscopy. Some authors recommend a simultaneous laparoscopy to minimize the risk of perforation; we think that systematic laparoscopy is not necessary and not that preventive. Good anatomical results are usually obtained. The hysteroscopic procedure is not aggressive and is sensitive to the surrounding endometrium, which is essential for a good anatomical and functional result. But also, Rochet¹¹ reported 72% positive results by several non-hysteroscopic techniques, controlled by hystero-graphy at 3-6 months after surgery. Some authors obtained 77.6% positive results only by the lysis techniques¹⁰. Hamou reports a success rate of 63,8% during the first sessions¹⁴. March and Israel¹⁵ had a success rate of 97%.

Valle and Sciarra find a recurrence in 48,9% the cases of severe adhesions, 21,6% for moderate but none for mild synechiae. After several treatments, the recurrence rate reached 35% for severe

synechiae and 5,2% for the moderate ones ¹⁶. Results of menstrual abnormalities are good: we get a significant improvement to symptomatology in 67% of the patients, especially in amenorrhea (80%). In 1250 and 775 cases, respectively, Schenker ⁸ and Siegler ¹⁷ note 84% and 87,2% positive results. Some authors obtain a 100% success rate for amenorrhea and hypomenorrhea ¹⁸. The results are correlated to the initial gravity of the lesions. The results of reproductive problems are still disappointing. They depend on the gravity of the disease but also additional infertility factors (uterine malformation, tubal sterility, sperm abnormalities). A good anatomical result is necessary, but not always sufficient. Most of the authors globally find disappointing results on reproductive problems, even if there is a relative disparity between the series. Only, Israel reports more optimistic series about exclusively corporeal synechiae ¹⁵.

Flexible plastic candles are used for curettage to minimize endometrial trauma, but still, Asherman Syndrome is a serious problem that we are dealing with it. Aim of treatment is to gain enough endometrial function and cavity after the success rate is lower than expected. Variety factors affect the success rate of treatment such as adhesion consistency and extensity, using IUD with or without hormonal therapy after the procedure, other fertility factors. Density and extensity of adhesions are important to expect the prognosis of the procedure. If the lesions are dense and highly fibrotic, they consist of massive scar tissue and no functional endometrial layer. The prognosis after curettage between second and fourth week of postpartum is also poor. Our hospital is a tertiary center, so mostly of our patients are more complicated than the normal population. This can be one of the causes of our unsatisfactory results.

Many authors support the concept of using IUD in the prevention of IUA. For this purpose, we used copper T 280 after adhesiolysis. We know that copper-bearing IUDs are not successful, because they have small surfaces and copper by itself can increase inflammatory reaction that can aggravate adhesion. For this purpose loop, IUD is the best choice, but in our country, there is no loop IUD. So we had to use copper T 280, which is a little more surface than copper T380A. In some studies, a Foley catheter with a three cc balloon was used for 15 days. Although the pregnancy rate was greater than the control group, infection rate, and also the pressure of the balloon on endometrium can increase adhesion formation after application.

In this study, a standardized pathway used for the operative and postoperative procedures to all patients. This is the major strength of our study. Also, another strength of our study is the long-term follow-up of the patients included in the study after hysteroscopic treatment. The most important limitation of our study is the retrospective nature of the study. The low number of subjects is also an important limitation.

CONCLUSION

Operative hysteroscopy is the best method to diagnose, classify, treat, and follow-up patients with IUA. Hysteroscopy must be the first choice in all cases with AS. Although a good anatomical result and the resumption of normal menstrual periods can be expected, the reproductive outcome is still disappointing. Restoration of a normal cavity and regular menstruation is not inevitably followed by normal fertility. Improvement of these results will depend on better management of additional infertility factors, early diagnosis, and treatment of initial lesions and their recurrences. But prevention is the best therapy by reducing uterine trauma as much as possible, particularly on a gravid uterus.

Prospective controlled studies are needed to determine the best diagnostic and treatment method of AS. The management of disease still poses a challenge. Close antenatal follow-up is necessary for women who conceive after treatment. It will be difficult to truly evaluate the usefulness of adjunctive measures until multicenter reports of successful treatments become available.

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