Understanding Intrauterine Adhesions: Hysteroscopic Evaluation

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Abstract
Intrauterine adhesion (IUA) or Asherman syndrome (AS) also known as uterine atresia, amenorrhoea traumatica, endometrial sclerosis is a challenging topic in the field of gynaecology, especially in the field of infertility. It is debatable in many aspects with no clear consensus about classification, management. The causes can vary according to geographical conditions and country to country. This article reviews the epidemiology, pathologic features, classification and management and the problems in all aspects. There are various predisposing, risk factors which can cause intrauterine adhesions. IUA caused by trauma to the basal layer of the endometrium characterized by variable scarring inside the uterine cavity. Trauma can be iatrogenic, infectious origin leading to amenorrhoea, hypo menorrhoea, infertility and placental abnormalities in pregnancy. Hysteroscopy is the gold standard for both diagnosis and management. Hysteroscopy has revolutionized the scenario of IUA. It is also important to prevent the recurrence of IUA with best available barriers like, hyaluronic acid, platelet rich plasma (PRP), stem cell therapy. Successful treatment of infertility achieved by complete restoration of uterine cavity, prevention of IUA reformation and promotion of healing process. Early diagnosis and treatment plays important role in preservation of infertility.

Keywords: Intrauterine Adhesion, Hysteroscopy, Infertility

Introduction
In 1894, Heinrich Fritsch described first case of intrauterine adhesions in a patient after postpartum curettage who presented with amenorrhoea. Subsequently, in 1948 and 1950, an Israeli scientist Joseph G. Asherman published two reports on the frequency and the aetiology of intrauterine adhesions.¹ He reported a case of severe intrauterine adhesions secondary to trauma to gravid uterus. He identified this pathology in 29 patients. These women presented with amenorrhoea with stenosis of internal cervical ostium. Two years later, with the help of hysteroscopy he published another case series of intrauterine adhesions. In this series intrauterine adhesions were involving uterine cavity. The prevalence of Asherman syndrome varies from 1.55 to 20%.² It depends upon population, country due to different diagnostic criteria, the number of abortions in the populations, the infectious diseases in that region, choice of management, awareness of clinicians and patients. Intrauterine adhesions (IUAs) are bands of fibrous tissue as a result of trauma to the basal layer of endometrium following pregnancy related curettage such as incomplete abortion, postpartum hemorrhage, and elective abortion³. Hysterotomy, myomectomy, caesarean section, hysteroscopic procedures like resection of submucous leiomyomata or septae, mullerian duct malformation, insertion of intrauterine device and endometrial ablation are less common factors which will cause IUA formation. In a country like India, genital tuberculosis is a frequent cause of intrauterine adhesion⁴. Puerperal sepsis is also common cause in some areas. It has serious clinical sequelae like infertility, recurrent pregnancy loss, menstrual abnormalities and pain. One should remember that, in the literature many cases reported that there were no symptoms even though patient was having IUA. Many times pregnancy after IUAs or after correction may be complicated by abortion, premature labor, placenta previa and placenta accreta. For initial diagnosis the less invasive Sonography, contrast sonohysterography or hysterosalpingography can be done and very useful. The final diagnosis is based on hysteroscopy. Hysteroscopy is gold standard in the diagnosis and management of IUAs.

Basic concept
The endometrium in the reproductive age female is an ever-changing structure with remarkable capacity to regenerate. It is divided into three layers-the stratum basalis, stratum spongiosum and stratum compactum. The stratum basalis is the deepest layer, changing little during menstrual cycle and left intact during menstruation but regenerate functional layer due to existence of endometrial stem cells. The endometrial stem cell niche⁵ (the microenvironment where stem cell regulation occurs) seems to be located at the endothelium of the spiral arterioles in the basal layer, providing support to both the epithelial and stromal compartments.⁶,⁷ This layer is important to the gynaecologist during any intrauterine procedure as well as any infection. As it has capacity of
regeneration, it maintains the menstrual cycle and fertility. If it is completely destroyed, further endometrial regeneration will not occur. The second and third layers are collectively considered the stratum functionalis. These are the layers that respond to ovarian steroids and are shed at the time of menstruation. The severity of IUA depends upon the damage of these layers.

**Clinical Challenges**

IUA is a silent enemy of reproductive women as well as treating gynaecologist. Challenges should cover identification of risk factors, primary prevention of adhesions, proper treatment and secondary prevention of adhesions after surgical treatment. It should also include anticipation of obstetric challenges.

**Risk factors, Epidemiology and what is happening exactly?**

Miscarriage accounts for 15% of clinically recognized pregnancies. 5% of women will experience two or more miscarriages during their lifetime.9 In the era of the medical method of termination like prostaglandins, many miscarriages are still being treated by dilatation and curettage (D&C). Apart from that use of sharp curettage or mechanical suction poses increased risk of many miscarriages are still being treated by dilatation and curettage (D&C). Apart from that use of sharp curettage or mechanical suction poses increased risk of AS and poor prognosis after surgical treatment. It should also include anticipation of obstetric challenges.

**Classification**

Many classification systems are described, with no universal acceptance of any one system and no validation of any of them. Hysteroscopy is the mainstay of both diagnosis and treatment, with medical treatments having no role in management.21

Since Asherman original description, there have been many attempts to find the most accurate classification for IUAs. Toeff and Ballas (1978) were the first authors who tried to classify AS on the basis of hysterosalpingographic findings.24

Type1- Atresia of the internal ostium without concomitant corporal adhesion.

Type 2- Stenosis of internal ostium causing almost complete occlusion without concomitant corporal adhesion.

Type 3- Multiple small adhesions in the internal ostium isthmic region.

Type 4- Supra isthmic diaphragm causing complete separation of the main cavity from its lower segment.

Type 5- Atresia of the internal ostium with concomitant corporeal adhesions.

In the same year, March et al.25 classified adhesions as minimal, moderate, or severe based on hysteroscopic assessment of the degree of uterine cavity involvement.
This classification is still used for its simplicity although it is considered insufficiently prognostic.

Mild- Filmsy adhesion occupying less than one-quarter of uterine cavity. Ostial areas and upper fundus minimally involved or clear.

Moderate- One-fourth or three-fourth of cavity involved. Ostial areas and upper fundus partially involved. No agglutination of uterine walls.

Severe- More than three-fourth of cavity is involved. Occlusion of both ostial area and upper fundus. Agglutination of uterine walls.

Hamou et al26 –Adhesions classified as isthmic, marginal, central, or severe according to hysteroscopic assessment. Valle and Sciarra27 used a classification based on uterine involvement observed in HSG, the extension and the type of adhesions seen on hysteroscopy and are described as follows:

- Mild: Fine adhesions, composed of basal endometrium
- Moderate: Fibromuscular, dense and endometrium covered adhesions that bleed when ruptured
- Severe: Composed of fibrous tissue, adhesions do not bleed when sectioned.

Wamsteker- The European Society of Hysteroscopy (ESH)28 proposed a classification of IUA as grade one to four with several subtypes based on HSG and hysteroscopy findings with clinical symptoms while the American Society for Reproductive Medicine (ASRM)29 also considered the menstrual pattern based on extent of endometrial cavity obliteration, appearance of adhesions and patient menstrual pattern.

Accordingly to score Mild(1-4), Moderate(5-8), Severe(9-12) [Fertil Steril 1988;49;944-55] The Donnez and Nisolle30 classified in six grades and consider the location to be one of the most important factors in determining the pregnancy rate after surgery. It includes:

- Grade I: Central; fine (IA) or fibrous or fibromuscular (IB) adhesions
- Grade II: Marginal adhesions; compact pillars (IIA) or obliterating one of the ostia (IIB)
- Grade III: Absence of cavity on HSG; occlusion only of the internal orifice (IIIA, pseudo-Asherman’s) or complete synechia of uterine walls (IIB, true Asherman’s)

Nasr et al31 suggested a complex system creating a prognostic score by incorporating menstrual and obstetric history with IUA findings at hysteroscopic assessment with HSG.

Evaluation

There are various modalities to evaluate the IUA. IUA can be visualized by hysterosalpingography (HSG), ultrasonography including contrast sonohysterography (SHG), 3D ultrasonography, hysteroscopy and magnetic resonance imaging (MRI).

Transvaginal 2D ultrasonography is the first-line diagnostic tool for the assessment of uterine and endometrial morphology. It assesses endometrial thickness, disruptions to the endometrial–myometrial junction. We can appreciate typical irregular endometrial line or at places it is absent. Sometimes hyperechogenic bridges can be seen. The typical ultrasound finding is the presence of hypoechoic areas with interruptions of the endometrial layer (skip lesions representing entrapped menstrual blood or secretions from preserved function endometrium).32 Adhesions on ultrasound are seen as bands of myometrial tissue traversing the endometrial cavity and adjoining the opposing uterine walls. The bands may vary in thickness, but their echogenicity is usually the same as that of the adjacent myometrium.33 It has been observed, in a study of 16 women with AS and 50 controls that, transvaginal ultrasonography in women with AS showed substantially thinner endometrium compared to normal menstruating women34. In cases of severe IUAs, the uterine cavity may appear irregular with a loss of endometrial echo.35 HSG can be used for diagnosis of AS. Advantage of HSG is that it will give graphical picture of uterine cavity as well as
complications, improving surgical outcomes and improving potential future fertility. Preoperative 3D-TVUS plays an important role in intra-operative judgment during hysteroscopic adhesiolyis.\textsuperscript{39} Magnetic resonance imaging has been used to investigate IUAs, especially when cervical obstruction is suspected, but experience with this technique is limited\textsuperscript{60,32}. Uterine synechiae can be visualized as thick or thin bands of soft tissue (signal intensity similar to myometrium on T1W and T2W imaging) that stretch from one wall to another.\textsuperscript{41}

**Preoperative preparations**

Misoprostol has been considered as a simple and effective method for cervical priming prior to hysteroscopy in IU with dose 200 or 400 μg vaginally prior to operative hysteroscopy. Twenty-five randomized controlled trials involving 2,203 females were systematically analyzed\textsuperscript{45}. As compared to placebo or no medication the use of misoprostol prior to hysteroscopy led to significant relief in cervical dilatation, fewer hysterectomy complications with mild and insignificant side effects.

**Treatment-**

IUAs are commonly treated with hysteroscopic resection followed by mechanical or hormonal treatments. Clinical challenges include primary prevention of adhesions, surgical removal, and prevention of recurrent disease. So the complete management can be divided into four main categories.

1. Surgical treatment- By hysteroscopy
2. Preventing recurrence of adhesions
3. Restoring normal endometrium
4. Second look Hysteroscopy-Postoperative assessment

**Surgical treatment**

It is always by hysteroscopy. Hysteroscopy is a wonderful technology giving clear access to diagnose the synechiae, to judge the extent of it, confirming location as well as type of adhesions (soft, muscular, fibrous). And in the same sitting treatment can be done. But we have to follow the principles to achieve the goals.

1. Restoration of the triangular cavity,
2. Visualization & confirmation of permeability of the ostiums
3. Avoid destruction to normal endometrium
4. Minimal manipulation
5. Avoid Perforation.

Importance to be stressed on proper indication and careful performance of intrauterine surgical procedures.\textsuperscript{45} Primary prevention as well as timely diagnosis and treatment seems to be crucial in the management of this pathology. To start with it is necessary to analyze the causative factors of Asherman’s syndrome, history of curettage (post-partum or for miscarriage) and any uterine surgery to be noted. Consider history of genital or extra genital tuberculosis diagnosed by acid fast bacilli (AFB) culture and/or histopathology especially in India. Difficulties can be encountered since beginning i.e. from the entry of hysteroscope through the external orifice till the negotiation through cervical canal, internal os to the uterine cavity. We can negotiate through the external cervical orifice with the help of 2.9mm hysteroscope and semirigid 5 Fr. scissors and forceps. The revolution in hysteroscopic instruments, optics and technology in last few years made hysteroscopy as the first choice.\textsuperscript{44,45} Filmy adhesions alone can be divided by using the tip of the hysteroscope without any energy source or scissors.\textsuperscript{45} Sometimes even with distension and pressure, but with patience, the filmy adhesions can be released. Thus, in favourable cases the restoration of cavity can be obtained through “no touch” hysteroscopy in out-patient setting without general anaesthesia.\textsuperscript{44} According to many experts, the removal of the adhesions should start form the lower part of the uterus and progress toward the upper part.\textsuperscript{46,32} Routinely the division of adhesions begins in the central and moves laterally and toward the fundus. So the central and filmy adhesions should be separated initially in order to allow adequate distension of the uterine cavity. Dense and lateral adhesions should be treated at the end, bearing in mind the greater risk of uterine perforation and bleeding\textsuperscript{47}. An effective way to recognize the margins of the original uterine cavity is to detect the myometrial vasculature by using the lowest intrauterine pressure and distension that allows visualization.\textsuperscript{49,50,51} A wide range of mechanical or electric equipment has been used for hysteroscopic adhesiolyis. Different hysteroscopic instruments are used like, 16-gauge, 80-mm Touhy needle (Portex Ltd., Hythe Kent, England) introduced alongside a 5-mm hysteroscope under fluoroscopic guidance\textsuperscript{52}, biopsy forceps, sharp or blunt scissors\textsuperscript{53,54} and division of string with energy like monopolar diathermia\textsuperscript{55}, bipolar diathermia\textsuperscript{56,49} or laser\textsuperscript{57}. Nowadays we are commonly using 2.9mm office hysteroscopes with 5 Fr scissors and forceps. (Fig. 1 to 6) Use of mechanical instruments like cold-knife is supposed to prevent thermal damage of the residual endometrium and reduce the rate of perforation during the procedure. Though the use of powered instruments (electric surgery or laser) has also proven efficient for hysteroscopic adhesiolyis,\textsuperscript{58} the use of electric surgical instrument is associated with potential damage to the residual endometrium.\textsuperscript{62,63} High frequency electrical surgical instruments (such as monopolar or bipolar electrocautery electrodes, resectoscopic electrocautery needles or loops) should be avoided for adhesiolyis in Asherman patients, in order to prevent deep local damage to the endometrium, though these methods for adhesive band vaporization have also been described. Bipolar surgery appears to be better than monopolar as tissue effect is more focal and the electrolyte containing distension media is safer concerning to fluid overload. So even monopolar surgery has provided results as satisfactory as bipolar one, the latter is more preferred.\textsuperscript{44} If thermal energy is used, the minimum amount of energy must be applied to minimize endometrial damage.\textsuperscript{65,66} A pilot study suggested the use of mini-resectoscope for hysteroscopic adhesiolyis is associated with reduced operative morbidity. Use of the mini-resectoscope is an effective and safe alternative to the conventional system.\textsuperscript{58} The treatment with laser vaporization using an Nd-YAG (neodymium-doped yttrium aluminium garnet) and KTP (potassium-titanyl-phosphate) laser has also been applied in the treatment of AS.\textsuperscript{65,66} But considering costs and increased uterine damages, it does not offer significant advantages over other electric equipment. Therefore its use in hysteroscopic adhesions has been increasingly abandoned\textsuperscript{45}. The treatment of the severe and dense adhesion is the real challenge as in these cases; the cavity may be completely
occluded or too narrow to allow the insertion of hysteroscopic sheath inside the cervix. Moreover, multiple procedures may be required because of post-surgical recurrence of the adhesions. Routinely mechanical methods are used widely. Mc Comb and Wagner in 1997 treated six cases with severe IUA under laparoscopic control: their technique was based on separation of uterine wall into two hemicavities by inserting a 13 French Pratt cervical dilator. Subsequently, the residual fibrotic “septum” was cut up to the fundus with hysteroscopic scissors. "Myometrial scoring" is an innovative technique, consists cutting six to eight incisions from the fundus of the uterus to the isthmus using a knife electrode with the aim of enlarging the uterine cavity and potentially uncovering functional endometrium. A transcervical resectoscopy after the dilatation of cervix with laminaria tent was also suggested in the treatment of severe AS.

In patients with suspected tuberculosis, one has to be very careful in adhesiolysis. Jai Bhagwan Sharma et al demonstrated the association between genital endometrial tuberculosis and Asherman’s syndrome. In a study of 28 women diagnosed as genital tuberculosis by endometrial biopsy, they did hysteroscopy. And they found, there were various grades of adhesions in all women, with grade I in 17.8%, grade II in 28.5%, grade III in 28.5% and grade IV in 17.5% women. Only four women (14.3%) had open ostia, while others had bilateral (28.5%) or unilateral (21.3%) blocked ostia or inability to see ostia (28.5%). In 70% infertile patients with GTB, cavity is normal with bilateral open ostia and normal looking endometrium. Classical hysteroscopic findings of endometrial TB is a rough dirty looking bizarre pale endometrium (Fig 13) with gland openings not seen and with overlying whitish deposits. After adhesiolysis many times cavity appears shrunken. (Fig 14). Sometimes there can be total corporal synechiae due to tuberculosis which carries a very poor prognosis. Adhesion dissection can be technically difficult and must be performed with care in order to not create new scars and further exacerbate the condition. In more severe cases, adjunctive measures such as laparoscopy are used in conjunction with hysteroscopy as a protective measure against uterine perforation. Microscissors are used to dissect as well as to judge and dilate to proceed forward smoothly. There are chances of uterine perforation following hysteroscopic lysis of synechiae due to tuberculosis.

![Fig 1: Circular Fibrosis at Internal Ostium](image1)

![Fig 2: Central adhesions just above internal os](image2)

![Fig 3: Judging with scissors](image3)

![Fig 4: Central Thick adhesions in the cavity](image4)
Fig 5: After cutting the band
(note the whitish endometrium)

Fig 6: Cavity after complete adhesiolysis

Fig 7: Second look after 3 months-same patient
(Note pink colour of the endometrium)

Fig 8: Second look- left lateral wall adhesions

Fig 9: Adhesiolysis with 5 French scissors

Fig 10: Releasing left lateral wall adhesions
Preventing recurrence of adhesions—Secondary Prevention

Any intrauterine surgery including adhesiolysis for IUA needs very careful approach to avoid reappearance of adhesions. Hysteroscopic adhesiolysis is necessary for restoring menstrual function and fertility. Apart from that future obstetric complications can be minimized with proper precautions. Since surgical wounds are prone to re-adhesion, the postoperative recurrence rate is as high as 3.1–62.5%. Especially in case of tuberculosis the chances are high hampering reproductive potential. The mechanisms by which the endometrium is repaired, are not entirely understood. The duration of endometrial healing also depends upon the pathology. A recent prospective study stated that the time needed for the endometrium to heal completely ranges from 1-3 months. Five RCTs are currently evaluating outcomes for secondary prevention strategies like an IUD, amnion graft, or stent, typically comprising an intrauterine catheter with an inflatable balloon tip, the use of gels such as hyaluronic acid and polyethylene oxide-sodium carboxymethylcellulose.

A-Intrauterine Device-
It was one of the first described method in literature it has been widely recommended in many studies. But few studies and AAGL practice report stated that there was no reported difference in rate of postoperative de novo adhesion formation assessed hysteroscopically, and there were no differences in pregnancy outcomes. Adding on, the uses of IUD with different shapes were also described as a possible treatment option. However, copper-containing uterine-shape and T-shape IUD can induce inflammation and are thus not recommended because of their insufficient surface area.

B-Foley’s Catheter-
It is also one of the first described in the literature. Eight observational studies report it as an alternative for this purpose. A pilot study done by Sahana Gupta et al shows no intrauterine adhesions with use of Foley’s catheter balloon (FB) for prevention of intrauterine adhesions following breach of uterine cavity in complex myoma surgery. At the time of follow-up hysteroscopy 6 months after the myomectomy, they found no intrauterine adhesions in 16 consecutive women treated with balloon, compared to 3 out of 10 (30 %) historical controls where the balloon was not used.
But a definite defect is noted in the FB. The shape of the balloon does not match that of the uterine cavity, and hence it cannot isolate the two sides of the uterine cavity and uterine horn accurately. The local pressure might affect the blood supply of the endometrium.98 Recently Christine Shan et al used Malecot catheter to prevent IUA. They found it is an inexpensive, easy-to-operate, and effective physical barrier method for preventing IUA in infertile patients undergoing hysteroscopic myomectomy with high live birth rate and no obvious visible post-operative adhesions.89,90

The intrauterine suitable balloon (ISB) is better than the Foley balloon (FB) in preventing the adhesion reformation and reducing the AFS (American Fertility Society) score after hysteroscopic adhesiolysis in severe IUAs. Also, it can effectively prevent the adhesion reformation in severe IUAs with a similar effect on moderate IUAs. 91

C-Intrauterine Balloon Stent-
March et al described intrauterine stent as a mechanical method to prevent adhesions recurrence. The author reported among 1240 patients treated using intrauterine stent, pregnancy rate of 61.6% and spontaneous miscarriage rate of 15.6%.92 Ru Zhu and Hua et al designed an intrauterine balloon stent and compared with Foley’s balloon.93 The device can effectively isolate the two sides of the uterine cavity and bilateral uterine horn, and it also consists of a drainage channel and an injection channel. The channels can sufficiently drain the exudate from the uterine cavity and inject the antiadhesion drugs into the uterus or promote the growth of the endometrium. Recently Huan Huang et al designed a novel intrauterine stent for prevention of intrauterine adhesions.94 In this design, the uterine stent fits into the normal shape of the uterine cavity and keeps the normal uterine cavity shape after surgery. Another RCT by X shi et al has demonstrated that following hysteroscopic adhesiolysis, the use of intermittent dilatation balloon therapy can significantly reduce adhesion reformation rates, while improving menstrual flow.95 Cook Medical (Cook Medical Inc., Bloomington, USA) introduced a intrauterine balloon, specially designed in a triangular-shaped form to simulate the uterine cavity. Most studies recommend that this balloon to be kept in the uterine cavity not more than a week due to risk of infection.96 In a comparative study Lin et al found that the insertion of an intrauterine balloon or intrauterine device is more effective than the use of hyaluronic acid gel in the prevention of intra-uterine adhesion reformation.97 But in 2015 Lin et al stated that the heart-shaped intrauterine balloon and IUD are of similar efficacy in the prevention of adhesion reformation after hysteroscopic adhesiolysis for Asherman syndrome.98

D-Word's Catheter-
The Word catheter is a 5.5cm length, 3ml balloon catheter of silicone with 15 French canal manufactured by Cook medical Inc. Bloomington USA. Jaimi Ferro et al proposed the usages of this catheter. 96 It acts as a foreign body preventing uterine walls to collapse as well as creates re-epithelization in the uterine cavity. It is placed in the uterine cavity with distal end slightly outside the cervical canal or at its border and inflated with 3-4ml of saline. The catheter can remain in position for at least 21 days and for up to two menstrual cycles. So the endometrium heals properly preventing the adhesions. There is no discomfort to the patient due to short tubing and the risk of ascending infection is less.

E- Anti-adhesion Barrier Gels-
Hyaluronic acid is one of the most widespread components in human tissue and it is involved in many biological functions such as mechanical support, cell migration and proliferation. It is a water soluble polysaccharide with known viscoelastic properties and works as a mechanical barrier between the uterine walls and prevents the development of adhesions. Autocross-linked hyaluronic acid (Hyalobarrier©) is a new anti-adhesion barrier capable of preventing adhesion formation after gynaecological surgery (Fidia Advanced Biopolymers SRL, Padova, Italy).96,99,100 Barriers methods are the most widely used and, among these, gel barriers have been proven to have a significant clinical effect on IUA prevention, because of higher adhesiveness and prolonged residence time on the injured surface (Level of evidence: 1b).101 Another modified hyaluronic acid (sodium hyaluronate) and carboxymethylcellulose (Seprafilm©) (Genzyme Corporation, Cambridge, MA, USA). In a randomized controlled blind study involving 150 patients who underwent surgical evacuation or curettage after missed or incomplete abortion, the rate of IUA in the treated group was low compared with the control group96 In a prospective randomized trial including 187 cases alginate carboxymethylcellulose hyaluronic acid was used and it was more effective than carboxymethylcellulose hyaluronic acid.102

Bosteels J et al101,105 conducted 11 randomised studies on use of an inserted device versus no treatment in 2015 and 16 RCTs in 2017 comparing a device versus no treatment. They concluded that, the effectiveness of anti-adhesion treatment for improving key reproductive outcomes or for decreasing IUAs following operative hysteroscopy in subfertile women remain uncertain. Another innovative study by Gretchen Garbe Collins et al suggested that amion graft may provide an alternative treatment option for patients with Asherman syndrome who desire future menses and pregnancy.104

Restoring the Normal Endometrium

A- Hormonal Treatment-
One of the most common therapies recommended is hormonal treatment. But there is no consensus about its usage as a sole treatment or in combination with other modalities; pre or post-operatively; combination of estradiol with progesterone and the duration of therapy.106 Yuqing Chen et al in their findings also revealed that, after TCRE and artificial menstrual cycle therapy for 3 months, the VEGF (vascular endothelial growth factor) expression and MVD(micro vessel density) increased significantly when compared with the IUAs patients before therapy and the controls. These findings indicate that estrogen may promote
the angiogenesis in the endometrium, which is helpful for the endometrial repair. Most of the studies recommended estrogen and progesterone after hysteroscopic adhesiolysis. Jolinda Johary et al reviewed and twenty-six studies were identified that reported use of hormone therapy as ancillary treatment after adhesiolysis. There was a wide range of reported menstrual and fertility outcomes. At present, hormone therapy, in particular estrogen therapy, is beneficial in patients with IUAs, regardless of stage of adhesions.

**B-Platelet-rich plasma (PRP)**

PRP is the plasma fraction of autologous blood with platelet numbers that are enhanced four- to six-fold compared with that of whole blood. Intrauterine infusion of PRP tried in many study trials. Jintao peg et al evaluated efficacy of an intrauterine infusion of platelet-rich plasma (PRP) in patients with intrauterine adhesions (IUAs). The mixture of PRP and PRP activator (with a ratio of 1:1) would be infused into the uterine cavity with a catheter for intrauterine insemination. There were no significant differences between the intrauterine infusion of PRP and the intrauterine balloon. However more RCT are needed. Meenu Agarwal et al tried the injection of platelet-rich plasma (PRP) guided by hysteroscopy into the endomyometrial junction on 32 patients of thin endometrium. They found it improves endometrial thickness and vascularity. After PRP instillation, the endometrium was 7 mm or thicker in 24 of 32 patients, and all 24 patients underwent frozen embryo transfer. Moreover, 12 of 24 patients who underwent embryo transfer conceived, whereas 10 had a clinical pregnancy with visualization of cardiac activity at 6 weeks and two had a biochemical pregnancy.

**C- Stem Cells Therapy**

Autologous stem cell implantation is an innovative therapy for endometrial regeneration in patients with AS. Endometrial regeneration from the basal layer, postulated to have stem cells or progenitor cells, contributes to the replacement of the functional layer. There is ample evidence that adult stem cell populations exist in human endometrium, and hence it might be possible to activate endogenous endometrial stem/progenitor cells in cases of atrophic or thin endometrium or to transplant bone marrow (BM) derived stem cells in the uterine cavity for endometrial regeneration in AS or severe cases of IUAs. In a study by Neetu Singh et al total of six women were included in the study and all of them had secondary amenorrhea with primary infertility. All of them had undergone hysteroscopic adhesiolysis (2-3 times) and received oral estrogens (2-3 cycles) in the past, but had failed to respond. Five out of six patients resumed menstruation after 3 months. The maximum ET achieved by any patient was 6.7 mm. Majority of the patients had a past history of treated genital tuberculosis (n = 5) and only one had a history of D and C. Santamaria X et al published a prospective study in 16 women and found improvement after two months with autologous cell therapy with CD 133+. Improvements were seen in endometrial thickness, increased mature vessel density and menses. This study also some promising pregnancy rates.

**Second look Hysteroscopy- Postoperative assessment**

In the management of intrauterine adhesions, it is very important to analyze the prevalence of IUAs in women undergoing intrauterine surgeries for intrauterine synechiae, polyp, submucous myoma. So evaluation of uterine cavity to diagnose and treat post-surgical adhesions with second look hysteroscopy is an essential part. Lauren Sebbag et al observed that IUAs occurred most commonly after hysteroscopic lysis of adhesion (26.9%) and myomectomy (20.5%), polypectomy (10.9%). They found that in 55.2% of cases, IUAs could be treated by second-look hysteroscopy. If initial stage of AS is more severe, then it is more difficult for the endometrial cavity to recover. So it is imperative to detect and treat adherence recurrence promptly to improve patient’s reproductive potential. In our case studies in last two years, six cases were with severe IUAs with secondary amenorrhea. Three of them had tuberculosis. We have achieved regular menstrual cycles in all cases and pregnancy in one case. One patient of 25 years was having amenorrhea for three years after D & C for missed abortion. She had good improvement in endometrium from white to pink. (See Fig 7-12)

Post-adhesiolysis- A significant improvement in the endometrial thickness was observed on day 2 (p < 0.0001) and day 21 (p < 0.0001) 3 months post-adesiolysis. The spiral artery RI was statistically significant (p < 0.04) on day 2 pre-adesiolysis compared to post-adesiolysis. Reproductive outcome following hysteroscopic adhesiolysis by K K Roy et al reported that in the majority (64%) of patients, the possible cause of Asherman’s syndrome was previous curettage on gravid uterus. The overall conception rate was 40.4% after hysteroscopic adhesiolysis.

Outcome of hysteroscopic adhesiolysis in women who had Asherman’s syndrome after uterine artery embolization (UAE) was worse than women who had Asherman’s syndrome caused by surgical trauma. Reproductive outcome in patients with tuberculosis is always guarded because by the time its diagnosis is done, major destruction already occurred.

**AAGL Guidelines for primary prevention of intrauterine adhesions**

1. The risk for de novo adhesions during hysteroscopic surgery is impacted by the type of procedure performed with those confined to the endometrium (polypectomy) having the lowest risk.
2. The method of pathology removal may impact the risk of de novo adhesions. Level B
3. The application of an adhesion barrier following surgery is impacted by the type of procedure performed with those confined to the endometrium (polypectomy) having the lowest risk. Level C

The application of an adhesion barrier following surgery that may lead to endometrial damage significantly reduces the development of IUAs in the short term, although limited fertility data are available following this intervention. Level
Post-Adhesiolysis Obstetric problems-

In dealing with patients of IUA, the clinician has to be alert when patient conceives after adhesiolysis. There was increased incidence (43.8%) of cesarean section. Four (12.5%) patients had postpartum hemorrhage for adherent placenta. There was no conception in patients who needed repeat adhesiolysis. - Placenta accreta: adherent placenta accreta. 119 - Placenta accreta: adherent placenta due to Asherman syndrome. 118 It is important to be aware of the risk of a placenta accreta if the patient is having previous history of Asherman syndrome and uterine scarring. And antenatal diagnosis is necessary so that counselling and mode of delivery can be planned. In the study of Limei Chen et al 7.9% had postpartum hemorrhage, including 4.3% due to adherent placenta and 2.1% due to placenta accreta. 119

Conclusion

As such, medical awareness seems to be important in minimizing the risk of IUA. Medical method for termination of pregnancy should be followed. The leading cause for Asherman’s is D and C done for abortion or RPOC. 120 If at all D & C is needed then sharp curettage to be avoided. Hysteroscopy is the most accurate method for diagnosis of IUAs and should be the investigation of choice when available. In developing countries like India Genital tuberculosis is an important cause of Asherman’s syndrome causing significant pelvic morbidity due to uterine adhesions and infertility. Primary prevention is very important and the operating surgeon should always consider the risk of adhesions according to type of endometrial pathology, avoidance of electrosurgery. To reduce the recurrence of adhesions after adhesiolysis, secondary prevention is necessary. According to availability clinician has to select judicially. Stem cell treatment may ultimately provide an effective adjuvant approach. Follow up assessment is required after two to three months. If the woman conceives after AS treatment, there should be vigilant surveillance and early diagnosis for placental abnormalities to avoid obstetric complications.

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References

2. Journal of Minimally Invasive Gynecology, Volume 17, Issue 5, September–October 2010, Pages 555-569; Review Article, Review of Intrauterine Adhesions Panel Rebecca Deans MBBS, MRANZCOG Jason AbbottB MED (Hons), MR-COG, FRANZCOG, PhD
3. Prevalence of uterine synecchia after abortion evacuation curettage; October 2007, Sao Paulo Medical Journal 125(5):261-4; Source-PubMed; Adriana Salzani, Daniela Yela, José Roberto, Erbolato Gabiatti, Ilza Monteiro
8. Recurrent miscarriage: Raj Rai 1, Lesley Regan Review Article, Published: 27 August 2008; Intrauterine adhesions(UA): has there been progress in understanding and treatment over the last 20 years?, Costas Panayotidis, Steven Weyers, Jan Bosteels & Bruno van Herendale Gynecological Surgery volume 6, pages197–211(2009)
11. Original Article, Published: 30 December 2017, The Expression of PDCD4 in patients with missed

14. Journal of Minimally Invasive Gynecology, Volume 24, Issue 1, 1 January 2017, Pages 74-79, Original Article; Prevalence and Impact of Chronic Endometritis in Patients With Intrauterine Adhesions: A Prospective Cohort Study panel Yuqing Chen MD, Li xiang Liu MD, Yuanna Luo MD, Minghui Chen PhD, Yang Huan MD, Ruili Fang MD


16. International Journal of Gynecology and Obstetrics 104 (2009) 49–52, CLINICAL ARTICLE Hysteroscopic findings in women with primary and secondary infertility due to genital tuberculosis Jai Bhagwan Sharma, Kalkol K. Roy, Mohanraj Pushparaj, Sunesh Kumar Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India


19. BJOG-an international journal of obstetrics and gynaecology, TRAUMATIC INTRA UTERINE ADHESIONS; Joseph G. Asherman, First published: December 1950


22. SM Journal of case Report, Feb 22 2017; Atypical case of Asherman Syndrome (Fritch Syndrome) due to prolonged Retained Fragment of Cu-T in Myometrium: Amera Anjum and Tabassum K

23. Elsevier-Journal of Minimally Invasive Gynecology, Volume 17, Issue 5, September–October 2010, Pages 555-569, Review of Intrauterine Adhesions, panel Rebecca Deans MBBS, MRANZCOG Jason Abbott B MED (Hons), MRCOG, FRANZCOG, PhD


35. Naftalin J, Jurkovic D. The endometrial–myomet-


73. Kumar A, Kumar A. Hysteroscopic findings of stary sky appearance and impregnated cobwebs in the endometrial tuberculosis. Int J Gynecol Obstet. 2014;126:280–1

74. Total corporal synechiae due to tuberculosis carry a very poor prognosis following hysteroscopic synechialysis; Orhan Bukulmez1, Hakan Yarali and Timur Gurgan+Author Affiliations Hacettepe University, Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara 06100, Turkey Received September 24, 1998. Accepted April 15, 1999

75. Uterine rupture following hysteroscopic lysis of synechiae due to tuberculosis and uterine perforation; Timur Gurgan1, Hakan Yarali, Biilent Urgan, Vural Dagli and Levent Dogan+Author Affiliations ;Division of Reproductive Endocrinology and Infertility, Faculty of Medicine, Department of Obstetrics and Gynecology, University of Hacettepe Ankara, Turkey; Received July 17, 1995. Accepted November 8, 1995


81. AAGL Practice Report: Practice Guidelines on Intrauterine Adhesions Developed in Collaboration With the European Society of Gynaecological En-


88. Taiwanese Journal of Obstetrics and Gynecology, Volume 59, Issue 1, January 2020, Pages 56-60; Intrauterine adhesion prevention with Malecot catheter after hysteroscopic myomectomy: A novel approach; Christine Shan-ChiChiuYaH-MingHwuabedRobert Kuo-KuangLieneabeMing-HuiLinaebd


94. Huang,1 Bin Xu,2 Chunxia Cheng, and Dabao Xu BJOG An International Journal of Obstetrics and Gynaecology, Gynaecological surgery; Prevention of postoperative adhesion reformation by intermittent intrauterine balloon therapy: a randomised controlled trial, X Shi, SH Saravels, O Zhou , X Huang , E Xia, TC Li, First published: 17 June 2019


Int J Clin Exp Pathol, v.6(7); 2013, PMC3693199, Int J Clin Exp Pathol. 2013; 6(7): 1343–1350. Published online 2013 Jun 15. Role of angiogenesis in endometrial repair of patients with severe intrauterine adhesion; Yuqing Chen,1 Yajie Chang,2 Shuzhong Yao1


Innovative Alternatives in the Postoperative Management of Asherman Syndrome; 42,438-445, Jaime Ferro, Pedro Montoya; Mastering techniques in hysteroscopy-R.e.book


Placenta accreta: adherent placenta due to Asherman syndrome; Line Engelbrechtsen, Jens Langhoff-Roos , Jens Joergen Kjer , Olav Istre; First published: 22 January 2015


Placenta accreta: adherent placenta due to Asherman syndrome; Line Engelbrechtsen, Jens Langhoff-Roos, Jens Joergen Kjer, Olav Istre; First published: 22 January 2015


Reproductive Outcomes in Patients With Intrauterine Adhesions Following Hysteroscopic Adhesiolysis: Experience From the Largest Women’s Hospital in China: Limei Chen 1, Hongwei Zhang 1, Qing Wang 1, Feng Xie 1, Shujun Gao 1, Yu Song 1, Jing Dong 1, Hua Feng 1, Kangyun Xie 2, Long Sui 3

International Journal of Current Research Vol. 10, Issue, 08, pp.72429-72434, August, 2018; Research Article Revisiting Diagnostic and Therapeutic Challenges in Asherman’s Syndrome: A Retrospective Analysis of 5 years. Richa Sharma, 2Rahul Manchanda and 3Nidhi Chandil

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