

Intrauterine adhesions (IUA): has there been progress in understanding and treatment over the last 20 years?

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Abstract We review the current evidence about the treatment modalities of intrauterine adhesions (IUA) or Asherman's Syndrome (AS). Systematic approach, audit and well-structured research is mandatory in order to establish the best treatment for the individual needs of patients. The clinical practice changed significantly over the last 20 years with technological advances in hysteroscopy and imaging techniques. Hysteroscopic treatment seems effective and safe. IUA or AS is a rather uncommon finding in general gynaecological practice. The referral to a tertiary centre will help to centralise the most difficult cases and create the opportunity to study more in detail the efficacy of

each treatment modality and to compare the different treatment techniques.

Keywords Intrauterine adhesions · Asherman's syndrome · Uterine synechia · Amenorrhoea · Infertility · Hysteroscopic adhesiolysis · Operative hysteroscopy

Background

In current gynaecology practice, intrauterine adhesions pose a difficult question concerning diagnosis and treatment modalities. Since the last 20 years few articles have reviewed this problem. Most of the literature is produced by tertiary centres focussing on fertility problems. This review aims to give an up-to-date information to the general gynaecologists and specialist residents, emphasises on the new therapeutic strategies and critically analyses the answered questions about future research on intrauterine adhesions (IUA).

History

Intrauterine adhesions (IUA) have first been described at the end of the nineteenth century. One of the first reported cases was from Heinrich Fritsch [1], a German gynaecologist and obstetrician, who in 1894 described IUA in a patient suffering from amenorrhoea following postpartum curettage. Asherman [2] studied similar cases and reported in 1950 the first large series of IUA. Since then different papers have been published reporting cases and treatment methods concerning IUA.

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Definition and symptoms of IUA

Intrauterine adhesions of the endometrial surface can be partial or complete. The terminology that should be used to describe these situations are the following:

Asherman's syndrome (AS) should refer to the complete obliteration of the uterine cavity with amenorrhoea as cardinal symptom [2, 3].

Intrauterine adhesions (*IUA*) or uterine synechias (synechia is a Greek word meaning continuation—adherence) should be used to describe partially adherent endometrial surfaces.

The clinical symptoms depend on the degree and the localisation of IUA in the uterine cavity.

Menstrual abnormalities are often reported: irregular bleeding, hypomenorrhoea, secondary dysmenorrhoea and amenorrhoea. AS is a rare entity and can be suspected, in case of secondary amenorrhoea, in a patient with a gynaecological history of a mechanical (curettage or manual) evacuation of retained products of conception.

In some cases, dysmenorrhoea and cyclical pelvic pains can be the only symptom. IUA obstructing partially or completely the isthmus or the internal cervical canal can cause secondary dysmenorrhoea or amenorrhoea, and haematometra can be formed. Increased menstrual reflux into the pelvic cavity through the tubes can provoke “de novo” pain or worsening of preexisting dysmenorrhoea. This clinical scenario is not that of an AS because the cavity is not completely obliterated and should be referred to as a particular localisation of IUA. Mild menstrual disorders or dysmenorrhoea can be masked by the use of oral contraception.

Retained menstrual debris could influence the rest of the endometrium, making it more vulnerable for de novo formation of IUA. However, this theory has not yet been proven. Normal menstrual patterns with subfertility [4] or recurrent pregnancy losses have been reported in association with IUA.

Subfertility can be explained in some cases by IUA. Obstruction of the tubal ostia at the uterine cavity side, inappropriate or insufficient endometrial surface for implantation or cervical obstructions are some of the causative mechanisms. IUA may be related with increased risk of miscarriage.

Sometimes IUA are found in eumenorrhoeic women [4].

Etiology, risk and associate factors

The endometrium has a unique capacity to regenerate its functional layer during the menstrual cycle. Different factors, however, can cause a destruction of the endometrium right through its basal layer into the muscle layers

of the myometrium. This destruction may not be repaired and leads to the formation of scar tissue (IUA). The etiology is not clear as the pathophysiology of the regeneration of the endometrial layers is not well elicited.

We could classify reported causative factors of IUA or AS as follows:

- Mechanical and iatrogenic complications such as curettage for miscarriage, manual removal of placenta, evacuation of retained products for incomplete miscarriages, hysteroscopic resection of polyps with excessive local destruction beyond the basal layer of the endometrium into the “compact zone” covering the myometrium, uterine septum resection [4] or myomectomy (hysteroscopic removal of multiple fibroids or abdominal myomectomy with opening of the uterine cavity [6]), uterine artery embolisation [7,8].
- Pathophysiological disturbance such as endometritis, complete miscarriage, septic abortion, uterine tuberculosis [9,10] Müllerian malformations, atrophy due to a long period of lactation [11] or menopause [12]
- Idiopathic when no apparent reason is found.

The types of the adhesion can vary from filmy to very dense, avascular, with a different degree of conjunctive tissue in growth. Presence of fibroblasts and atrophic endometrial cells can be found as well. Adhesions can have their origin from the endometrium, myometrium or connective tissue. Muscular adhesions can be present when there is no endometrium basalis [13]. Dense fibrotic adhesions do not have any endometrial lining [14]. We do not know if adhesions are part of the physiological remodelling of the endometrial cavity or if their existence is always pathological and should always be correlated with a local factor of disturbance such as endometritis. When significant clinical signs are present severe intrauterine adhesions are nearly always encountered. However, we do not know the natural evolution of these adhesions. We do not know if adhesions can be present for transitory periods and disappear later. Furthermore, it is uncertain whether or not there is a pattern for a further development, a worsening evolution and finally if any present IUA in the uterine cavity will form at some point an AS. The lack of evidence at the pathophysiological level makes the choice for an effective treatment more difficult.

The diagnosis

Women with IUA seeking help from the gynecologists may present different clinical manifestations from menstrual disorder dysmenorrhoea to hypo-fertility. The presence of IUA can be suspected, taking into account relevant

information from a thorough personal patient history aimed to identify previous gynaecological infections, pelvic inflammatory disease, iatrogenic correlated complications, obstetrical complications and history of pelvic tuberculosis. However, IUA is considered as a rare pathological entity and its prevalence is very difficult to estimate. It depends on the population under study. In countries where genital tuberculosis is more prevalent, AS or IUA are more frequent [9]. In populations where more curettages or abortions are performed, IUA or AS may be more frequent [15]. The incidence depends from the diagnostic modalities and scrutiny of investigations. While incidence seems to increase as a result of better awareness of the condition by the general physicians and gynaecologists, it is of importance to realise that the incidence of pregnancy interruptions has also increased despite intense efforts of effective family planning measures and contraception. In 13% of women undergoing routine infertility investigations AS has been found [16].

Manual removal of placenta is considered to be a risk factor (with subclinical infection after manipulation or mechanical trauma). Hysteroscopic evaluation after manual removal of placenta has diagnosed IUA in 2% of the cases [17]. Fifteen to thirty percent of the patients in which evacuation of retained products of conception for incomplete miscarriage was necessary, have been reported to have IUA [8, 18, 19]. Some reported an incidence of 40% at hysteroscopic control 3 months after dilatation and curettage (D&C) for miscarriage [11]. Women who had previous caesarean sections [16], a placenta accreta [16], a uterine rupture or a postpartum endometritis are at greater risk to develop IUA or AS [16]. The age of the patient plays a significant role in the occurrence of IUA. Older women, over 35 years of age, have a higher risk to develop IUA in case of endometrial trauma compared to younger women [16].

Investigations leading to diagnosis of IUA

The gold standard for the diagnosis of IUA and AS is hysteroscopy since it offers a direct view of the IUA.

Hysterosalpingography (HSG) may suggest cervical obstruction (Fig. 1). The internal endometrial pattern is not predictive of the presence of adhesions. Transvaginal ultrasonography (TVS) can demonstrate hyperechogenic areas correlating with dense adhesions. TVS has high specificity but widely varying sensitivity. TVS that is performed on women of high risk for IUA formation can have very good accuracy and is very useful as screening test prior to hysteroscopy [20, 21]. Preoperative endometrial thickness as determined by TVS appears to have prognostic value in cases of severe Asherman's syndrome [22]

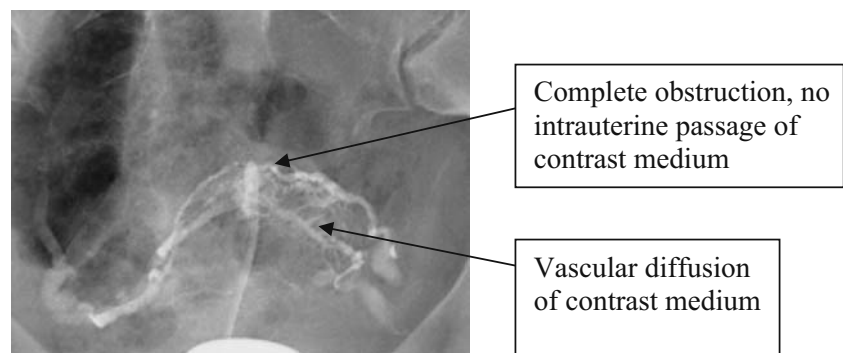
Recent TVS studies demonstrated very thin endometrium and absence of haematometra in most women with uterine outlet occlusion by IUA—AS [23]

Recently it has been stated that saline infusion sonography (SIS) had a higher level of correlation with hysteroscopic findings than TVS [24, 25]. SIS and HSG may have similar sensitivity with high false-positive rate [10, 25, 26]. Three-dimensional sonohysterography [27] and magnetic resonance imaging [28] may represent a newer diagnostic modality for IUA, which is under evaluation as its limited application. Office hysteroscopy after HSG or SIS [29] can confirm the presence or absence of IUA. Moreover, office hysteroscopy offers the possibility for immediate treatment. Appropriate setup with adapted instruments and resuscitation provisions is mandatory in order to avoid complications and conversion to a procedure under general anaesthesia [30].

Classifications

Different scoring systems have been described in order to classify the severity of the adhesions [3, 31, 32]. These different classifications are shown in Tables 1, 2, 3 and 4. The aim of these classifications is to bring a systematic evaluation of the diagnosis, the prognosis and the treatment outcome. These classifications use hysteroscopic view as main criteria. Clinical manifestations of IUA are added in order to have a clinical input in the classification aiming in a more comparable scoring system. The American Society

Fig. 1 Hysterosalpingography: complete obstruction of the cervix, uterine vascular diffusion of the contrast medium



Complete obstruction, no intrauterine passage of contrast medium

Vascular diffusion of contrast medium

Table 1 Classification of IUA by the American Fertility Society, 1988

	Characteristics		
	<1/3	<1/3–2/3	>2/3
Extent of cavity involved	1	2	4
Type of adhesions	Filmy	Filmy and dense	Dense
Menstrual pattern	Normal	Hypomenorrhoea	Amenorrhoea
Prognostic classification		HSG score ^a	Hysteroscopy score
Stage I (mild)	1–4	– ^b	– ^b
Stage II (Moderate)	5–8	– ^b	– ^b
Stage III (severe)	9–12	– ^b	– ^b

^a All adhesion should be considered dense.

^b Additional findings

for Reproductive Medicine's subsequent classification of IUA includes the extent of endometrial cavity obliteration, the hysteroscopic appearance of adhesions as well as the degree of menstrual disturbance [32]. Other classification system includes previous obstetric history [33]. However, these classifications are not comparable one to another. This makes evaluation of treatment outcomes rather difficult in the different reported cases. An empirical hysteroscopic description is the main criterion taken into account for the assessment of the degree and score of the adhesions. The European Society of Hysteroscopy (1989) classification is more useful to evaluate clinical symptoms. The reported results should have a thorough description of the hysteroscopic findings and the menstrual pattern of the patient in order to compare the different reported case series and, by consequence, the different classification scores.

Treatment

The aim of an adhesiolysis or synechiolysis is to restore the functional anatomical volume of the uterine cavity and free

Table 2 Classifications of IUA and AS following Valle and Sciarra, 1988

Grade	Findings
Mild	Filmy adhesion composed of basal endometrium producing partial or complete uterine cavity occlusion
Moderate	Fibromuscular adhesions that are characteristically thick, still covered by endometrium that may bleed on division, partially or totally occluding the uterine cavity
Severe	Composed of connective tissue with no endometrial lining and likely to bleed upon division, partially or totally occluding the uterine cavity

Table 3 Classifications of IUA by the European Society for Hysteroscopy (ESH), 1989

Grade	Extent of intrauterine adhesion
I	Thin or filmly adhesion Easily ruptured by hysteroscope sheath alone Cornual areas normal
II	Singular firm adhesions Connecting separate parts of the uterine cavity Visualization of both tubal ostia possible Cannot be ruptured by hysteroscope sheath alone
IIa	Occluding adhesions only in the region of the internal cervical os Upper uterine cavity normal
III	Multiple firm adhesions Connecting separate parts of the uterine cavity Unilateral obliteration of ostial areas of the tubes
IIIa	Extension scarring of the uterine cavity wall with amenorrhoea or hypomenorrhoea
IIIb	Combination of III and IIIa
IV	Extensive firm adhesion with agglutination of uterine walls At least both tubal ostial areas occluded

the ostia of the tubes. Ideally, the destruction of the IUA should be followed by recolonisation of the uterine cavity by the remaining normal endometrium. However, this is not always the case after one intervention and repeated hysteroscopic adhesiolysis may be necessary. The improvement of the menstrual pattern with more abundant periods is an encouraging clinical finding but is not always correlated with an improved fertility potential. Investigation methods such as hysterosalpingography or sonohysterography cannot evaluate directly the endometrial cavity. These imaging methods give an overall impression of the shape or form of the uterine cavity. Therefore, a hysteroscopic postoperative reevaluation is preferred in order to assess the quality of the endometrium and the possible need for further hysteroscopic adhesiolysis.

Table 4 Classifications of IUA and AS by Donnez and Nisolle, 1994

Degree	Location
I	Central adhesion (a) Thin filmy adhesion (endometrial adhesions) (b) myofibrous (connective adhesions)
II	Marginal adhesions (always myofibrous or connective) (a) Wedge-like projection (b) Obliteration of one horn
III	Uterine cavity absent on HSG (a) Occlusion of the internal os (upper cavity normal) (b) Extensive coaptation of the uterine walls (absence of the uterine cavity; true Asherman's syndrome)

Techniques of adhesiolysis

Intrauterine adhesions can be different in intensity. Some are filmy and can be separated during the diagnostic hysteroscopy using the barrel of the scope without any difficulty (Fig. 2); others, however, are more symmetrically formed in a shape of columns mainly on the lateral sides of the cavity. These can be separated successfully with three to four incisions in the lateral walls from fundus to isthmus and two to three transversal incisions for mainly fundal IUA. The most difficult cases are the dense adhesions (Fig. 3) that feel hard on hysteroscopic palpation. These have an arch-form aspect. These adhesions may need higher energy to be separated. It can be difficult to distinguish between abnormal endometrium and healthy areas depending on the extension of the adhesions, the presence of vessels and their consistence (whitish fibrotic areas versus atrophic endometrial areas) (Fig. 4).

Scissors

Mechanical separation of IUA is the most accessible mean of adhesiolysis in an appropriate setting for office operative hysteroscopy (Figs. 5 and 6). It offers significant advantages:

- Direct view and symmetrical separation of the adhesion without destruction of the normal endometrium present in the proximity of the IUA.
- Easier insertion of the hysteroscope in the uterine cavity in case of cervical obstruction. Two to three lateral incisions or in X shape (Fig. 7) in the cervical canal can facilitate the passage of the scope and allow further treatment higher up in the uterine cavity.

Vaginoscopy and office hysteroscopy gained more and more popularity the last years. Some important technical tips regarding office operative hysteroscopy [30, 34, 35]:

- Avoid the use of a speculum combined with a cervical tenaculum that can distort the normal axis of the cervix

jeopardising a cervical perforation during dilation or hysteroscopic entrance. It is not the speculum but the traction of the tenaculum on the cervix that leads the operator to believe that the uterus lies in the same axis as the hysteroscope. In experienced hands, vaginoscopy—no-speculum hysteroscopy—prevents trauma and can help in severe cases of IUA or AS to avoid perforation that may be caused if the cervix is maintained in a non-natural axis.

- Avoid the need for cervical dilators, diminishing the local mechanical trauma
- During adhesiolysis, the operator should stop if minor bleeding appears. This symptom corresponds to the passage into the healthy vascularised tissues. This point is important to consider as more bleeding and the destruction of potentially healthy tissues will provoke secondary adhesions. This final limit is not easily seen with other energy sources. It makes the scissor adhesiolysis the least aggressive method for the surrounding endometrium and myometrium

Laser

Yttrium-aluminum-garnet (YAG) laser fibre dissection is of great value for the adhesiolysis (Fig. 3): the tip of the fibre is visualised and guided to dissect the adhesions. However, in a completely obstructed cavity, this energy is very difficult to be used without orientation. The laser takes very little time to dissect lateral wall adhesions. The technique should be applied very delicately as fibres are very fragile and expensive to replace. In experienced hands, laser can be very effective with minimal tissue destruction. However, be aware that heat diffuses into the tissues, causing thermal damage up to 1 cm in depth and bubbles may be present during dissection hindering the view. Good view is essential in operative hysteroscopy. YAG laser use for minimal access surgery however is very expensive and not readily available in all hospitals. Few reports have included YAG laser use for IUA dissection [36].

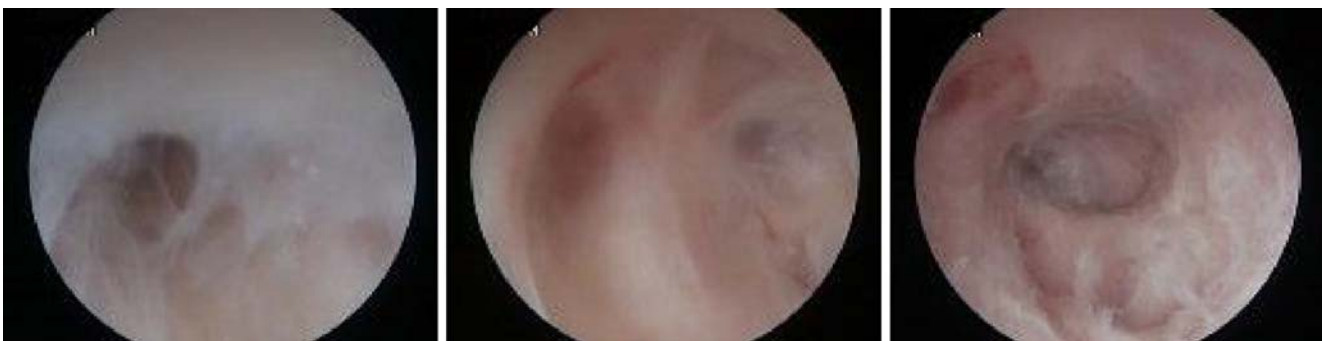


Fig. 2 Outpatient hysteroscopy: filmy adhesions, separated using only the edge of the hysteroscope

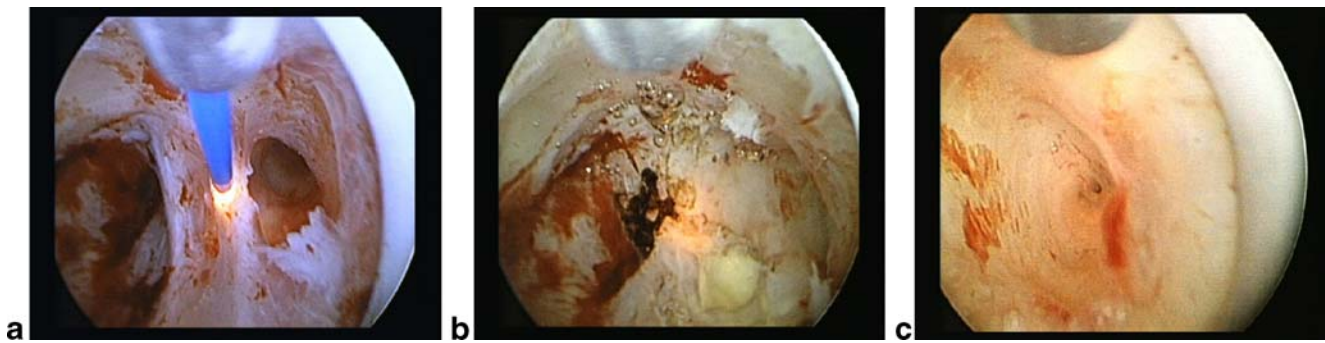


Fig. 3 Same patient of Fig. 2 during operative hysteroscopy. **a** Laser lysis of thick adhesions. **b** Reconstruction of uterine cavity. **c** Right ostium liberated

Monopolar or bipolar electrosurgery

Resection with electrical power is the most frequently used method. Bipolar energy has the advantage that normal saline can be used as distension medium decreasing the risks of fluid absorption and possibly allowing the operator more time for the treatment of the IUA. There is, however, also an effect of heat on the local healthy tissues: electricity has an in-depth penetration of 0.6 cm at a setting of 120 W. All measures to limit the destruction to the IUA should be made. Resectoscopes initially have been designed for destruction of endometrium in case of dysfunctional bleeding. The technique can be applied gently in a focussed way for the destruction of the IUA (Figs. 8, 9, 10). The risk of perforation has to be taken into account in cases of severe IUA or AS. There are no visible anatomical markers left in these cases causing a claustrophobic effect thus not allowing for a proper orientation. More recently, smaller bi-polar electrodes do allow separation of adhesions without anaesthesia using the vaginoscopic technique according to Bettocchi [34].

Pressure lavage technique

This technique is based on the sonohysterographic principle using saline solution injection under ultrasonic observation. Accumulation of saline in the uterine cavity can dilate and

mechanically disrupt IUA [37]. This technique is applicable for mild to moderate filmy adhesions.

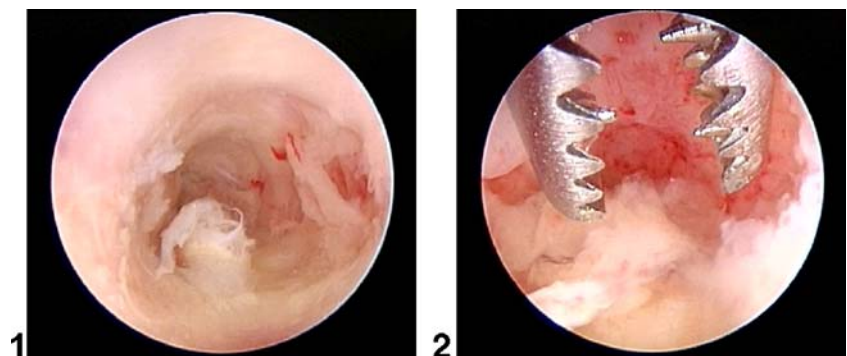
Modified uterine catheters

These catheters permit a simultaneous passage of a hysteroscope through the cervix [38]. The balloon at the end of the catheter distends the endometrial cavity. The possibility to have a hysteroscopic view whilst experiencing a tactile feeling with the balloon gives the advantage of the direct observation on IUA separation. At some instances it permits the use of scissors to facilitate the synechiolysis. These techniques are applicable for mild partial adhesions rather than for the dense ones. The pressure effect of the balloon cannot be limited to the IUA areas causing a possible destruction of the neighbouring normal endometrial areas. This may delay the recolonisation of the endometrium in the case of severe IUAs.

Fluoroscopically guided technique

With this technique the adhesiolysis is performed under general anaesthetic, with the use of a spinal needle in parallel to the hysteroscope. The progress of the procedure is determined by injecting radiographic contrast medium, and visualised with the use of an image intensifier [38–40].

Fig. 4 Complete IUA (1) in a patient with uterine tuberculosis. Adhesiolysis with scissors and grasper (2). Vascular endometrium can be distinguished (2)



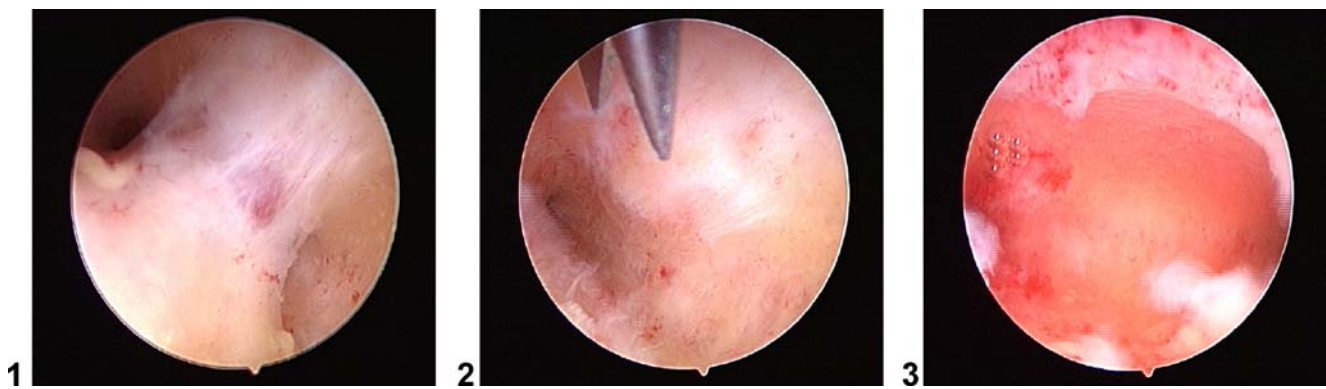


Fig. 5 IUAs, middle uterine cavity (1) liberated by scissors (2). Uterine fundus if free at the end of the procedure (3)

Intraoperative complications

In AS and severe cases of IUA, perforations during dilatation have been reported in 7% [16] and during dissection in 1–3%. During the hysteroscopic adhesiolysis a diagnostic laparoscopy can simultaneously be performed in order to prevent possible perforation. In ideal circumstances, the operator may be able to see the form and detect changes on the uterine surface before any perforation may occur. However, the risks of laparoscopic entry techniques should be taken into account. Furthermore, the angle of the uterus is not the same for the laparoscopist as for the hysteroscopist and therefore the observation of the uterus is

much more difficult in these cases than when the uterus is elevated during diagnostic laparoscopy. Perforation may be detected only in the fundal parts of the uterus. The use of laparoscopy can have the additional potential to investigate the pelvis in case of infertility problems and perform a dye test to confirm tubal patency. In cases where only menstruation is expected as an outcome, laparoscopy is not needed.

Simultaneous abdominal ultrasound scan with half-filled bladder during adhesiolysis is an easier technique to prevent perforation as the tip of the hysteroscope is visualised and its distance from the myometrium can be measured.

Fig. 6 Different types of scissors cutting IUAs



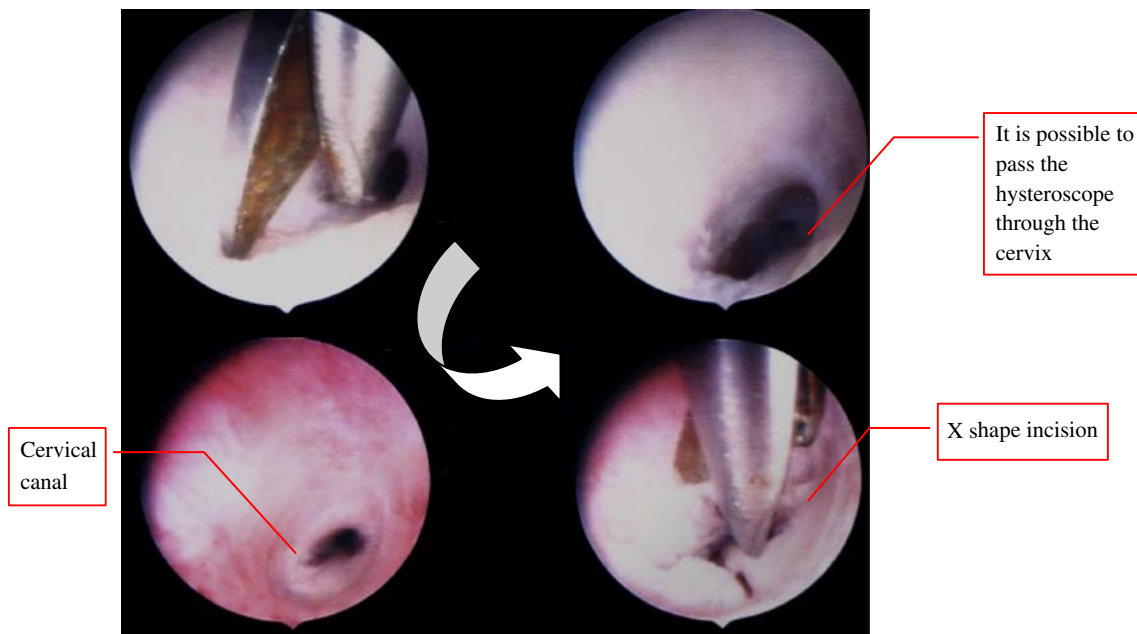


Fig. 7 Use of scissors, opening the intra-cervical canal. Note that no passage was present initially and with X-shape incision adequate passage was achieved

The use of these additional aids has to be tailored to the individual case. Experience and careful dissection technique, with good preoperative assessment and choice of adequate material for use, are important factors influencing the perforation rate.

Use of fluoroscopy can be considered in cases of severe IUA or AS. Pseudo-pockets of adhesions in AS can be radiographically detected and help the oriented dissection of these areas lowering the risk of perforation [38–40]. Severe AS lysis should only be attempted in fully equipped theatres with the possibility to switch from ultrasound to radiology or laparoscopy during the same session.

An additional advantage of fluoroscopic technique of adhesiolysis is the possibility to perform tubal patency test avoiding a laparoscopy or a subsequent need for

hysterosalpingography. However, an image intensifier and an experienced radiographer are not readily available in most operating theatres. The use of intraoperative antibiotics is mandatory.

Postoperative care

Adjuvant therapy with high-dose oestrogens with or without progestogens

There is no evidence from randomised studies that hormonal therapy with high doses of oestrogen will accelerate the re-epithelisation of the uterine cavity or that it may affect the survival of the endometrial cells after local destruction of IUA. Although the endometrium is hormone-dependent, most of the patients do have an adequate ovarian function, and it remains questionable if adjuvant oestrogen therapy will improve the menstrual outcome. The use of oestrogens is empirical and no datum exists concerning the dose and the length of therapy. Most authors used 1–3 months of a high dose of oestrogens [37, 38, 40]. Progesterone test can be used to induce the menstruation if it does not occur spontaneously.

Copper intrauterine device (IUCD)

There is no evidence suggesting that the use of IUCD can prevent the reformation of IUA or that it helps the epithelial recolonisation. On the contrary, due to its local inflamma-

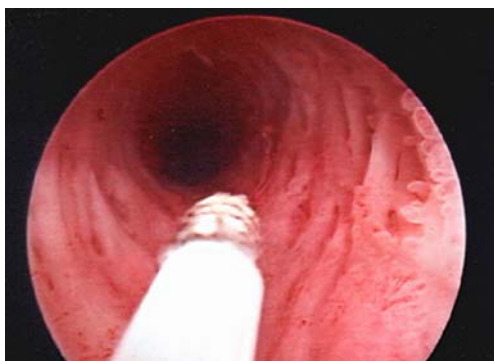


Fig. 8 Versapoint® bipolar electrode used for adhesiolysis on cervical adhesions

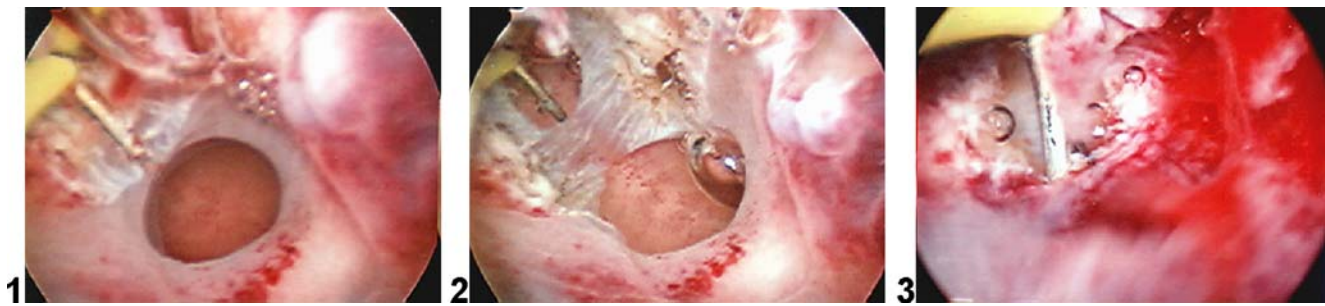


Fig. 9 IUA adhesiolysis using monopolar electrode. Normal endometrium is distinguished in the centre—fundus (1–2). Adhesiolysis stops when vascular endometrium is exposed (3)

tory action the IUCD may disrupt a normal endometrial colonisation even if the uterine walls are not in contact. The removal of the IUCD a couple of months postoperatively should be done very gently in order to avoid any endometrial trauma during its retrieval. The initial reports may have had promising results on mild to moderate cases of IUA where normal endometrial surface may have exceeded the surface of the IUAs. Reports of non-use did not show worse results in terms of fertility or menstrual function [8, 41].

Intrauterine catheters

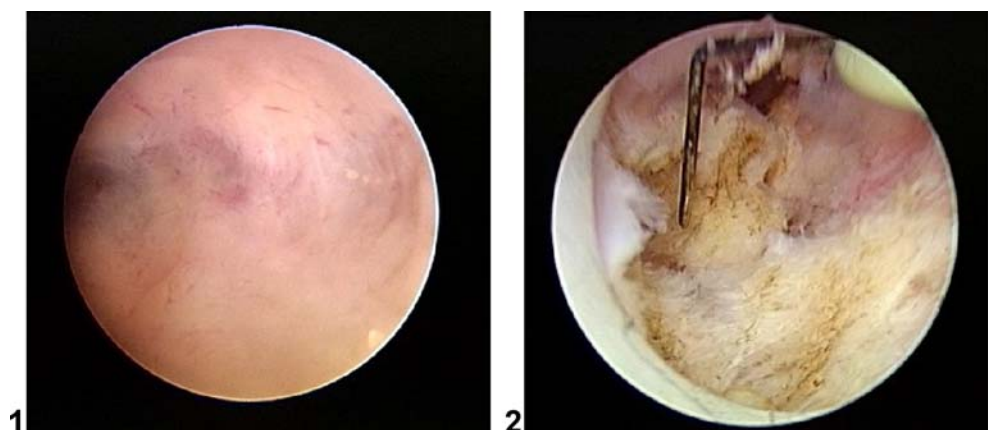
Foley's catheters or intrauterine balloons were suggested as another mechanical method that could prevent the immediate reformation of adhesions during the postoperative period. Patients may need to be hospitalised for a couple of days [42, 43] or to preserve the catheter for longer periods as outpatients [44]. The removal of the catheter can be done safely in the gynaecological outpatient clinic. In case of long-term use of an intrauterine catheter in situ, patients need to take long-term antibiotic therapy with possible side effects (gastrointestinal, bacterial resistance). Recently, it was advocated that the use of a Foley's catheter in

comparison with IUCD may have better results concerning postoperative menstrual pattern [44].

Follow-up

When the adhesiolysis did not restore a “satisfactory” endometrial cavity further procedures are needed. To evaluate the results of the adhesiolysis before further management, a local assessment of the uterine cavity is mandatory. No consensus exists about when a follow-up exam has to be planned or about what to use for this evaluation. Hysterosalpingography can determine tubal patency but not the quality of the endometrium. Outpatient hysteroscopy is more practical in appropriate organised outpatient set-ups and avoids general anaesthesia. The length of time between operation and hysteroscopic reevaluation may play a role on the observed endometrial aspect. If the hysteroscopy is done too early after surgery the endometrial healing may not be completed. On the other hand, if the hysteroscopy is done much later (in cases of incomplete adhesiolysis), performing the latter may not demonstrate a significant benefit, as a further procedure will be necessary. In severe AS cases, reformation of adhesions

Fig. 10 IUA after 3 months post curettage (1). Adhesiolysis with monopolar electrode (2)



can be observed [43]. A systematic approach for objective evaluation of the endometrial cavity is needed in order to determine the optimal time interval and the usefulness of these techniques.

If the treatment aims to improve patient fertility and repeated hysteroscopic procedures have been performed for this reason, it is of great importance to monitor these patients closely in a follow-up scheme.

Prevention of IUA or AS

Prevention has to be based on the minimal destruction of the physiological environment of the endometrial cavity. In cases of pregnancy termination and management of miscarriages, the use of a medical approach could decrease the risks of mechanical trauma and consequently the risks of IUA. However, the impact of medical treatment on the formation of IUA is unknown.

The preventive use of vaginal misoprostol for inducing cervical softening may avoid difficult cervical dilatation prevent cervical trauma that can lead to stenosis (when vaginoscopy—no-speculum hysteroscopy or 5-mm hysteroscope—are not available). A cheaper option is the use of laminaria-type dilators (Dilantin®) prior to an operative hysteroscopy in selected cases. Classical laminaria do swell above the cervical canal (Isthmus) if brought in too deep and can therefore be difficult to remove. The physician has to use the laminaria that have a “memory” and do swell evenly over their total length.

Antibiotic therapy is mandatory after intrauterine manipulation for obstetrical complications such as manual removal of placenta or curettage and in operative hysteroscopic removal of multiple myomas. More cases of IUA or AS are correlated with postoperative infectious complications such as endometritis.

In the case of treated endometritis, the postoperative diagnostic hysteroscopic assessment may be of value in order to detect early filmy IUA and treat these accordingly. This policy may avoid further development of more severe IUA, which are more difficult to excise.

Amenorrhoea during prolonged lactation rarely provokes IUA formation [11]. It is unknown if this rare observation can be associated with the prolonged use of progesterone pill or an undetected minor postpartum infection. Breast-feeding should be encouraged and most of the mothers tend to breastfeed their babies for a couple of months (few however for longer periods in developed countries). Breast-feeding increases contractions of the uterus, which enhances the spontaneous evacuation of lochia. In appropriate organised units, a hysteroscopic evaluation of the endometrial cavity could be informative for research needs in case of prolonged amenorrhoea due to lactation (for example

amenorrhoea more than 12 months). Successful family planning, education about and awareness of different contraceptive methods and easy access to gynaecological advice should help to decrease the number of terminations that are currently practiced. The organised early pregnancy units and family planning clinics will play a paramount role in the future for the above purposes.

Technological advances in recent years allow the use of smaller hysteroscopes facilitating hysteroscopic examination in an outpatient setting [34, 45]. Early detection of IUA may improve management strategies. Women who had puerperal surgical evacuation of retained placenta tissues, proved to have an increased risk of IUA formation (up to 40%) during hysteroscopic assessment 3 months post-operatively [11]. An early hysteroscopic assessment could detect and treat IUAs avoiding worsening synechia formation.

Auto-cross hyaluronic acid gel [46] was proposed as a mean of prevention of IUA. Amnion graft following hysteroscopic lysis of IUA was recently proposed as another option in order to decrease recurrence of IUA after treatment and facilitate the re-epithelisation of the uterine cavity [47]. Further studies are needed to evaluate long term these options for both modalities.

Objective outcome measures

Menstruation and fertility

Improvement of menstrual blood flow is the end result in most cases of adhesiolysis varying from 80% to 96.8% [8, 40, 43, and 48]. Pregnancy rates after final adhesiolysis for IUA or AS may be successful up to 53% [40] or 63% [43]. Some have reported pregnancy rates of 93%, 78% and 57% after treatment of mild, moderate, and severe adhesions with live-birth rates of 81%, 66% and 32%, respectively [31]. Fertility and live births outcome is very difficult to establish in long-term duration studies. The overall pregnancy rate may approach the 60% and the live birth rate up to 38.9%, depending upon the severity of the IUA [49]. However, the age of the patient seems to play a very important role.

In younger women (less than 35 years of age), the fertility rate after adhesiolysis for severe IUA or AS can achieve 62% [16] or 66% [8]. If the woman's age is more than 35, the fertility rate is reported to be much lower: 16% [16] to 23% [8]. Adhesiolysis of IUA in women with recurrent pregnancy loss leads to improved pregnancy rates (pregnancy rate 70–80%) [31, 43] in comparison with women treated for infertility. Patients treated for moderate or severe adhesions should be considered at risk and need a referral to a tertiary centre; if pregnancy occurs following

the treatment it should be considered as a high-risk pregnancy. Pregnant patients after AS treatment do present more miscarriages in the first and second trimester [16].

Therefore, cerclage could be a preventive measure that needs to be considered [8, 16]. AS treatment is a significant risk factor for placenta accreta or increta [50]. Placenta accreta may be present up to 9–22% in subsequent pregnancy [16]. Uterine dehiscence in the last trimester, from 35 weeks onwards and uterine rupture is another potential serious obstetrical complication of pregnant women treated for AS [16, 51].

Pain

If there is obstruction of the endo-cervical canal or the uterine isthmus, the patient may progressively present dysmenorrhoea and haematometra (Fig. 11). The hysteroscopic resection of these IUA will treat this problem restoring the menstrual outflow through the lower part of the uterus and will significantly decrease menstrual pain.

Other rare cases of IUA or AS

Müllerian malformations can provoke stagnation of menstrual debris or old blood inside the uterine cavity. Endometrial reaction to this event can be visualised (Fig. 12). Stagnation of menstrual material may provoke inflammation and a secondary adhesion formation. During hysteroscopic investigation of müllerian abnormalities some degree of IUA can be visualised.

AS or IUA can be detected during menopause. Sometimes extreme atrophy can cause the endometrial walls to adhere. Most of these cases are asymptomatic. However, there is the potential risk of postmenopausal bleeding not revealed in the case of an isthmic or cervical obstruction. Transvaginal ultrasound has limitations as the endometrium in AS may not be identified and if hyper-echogenic area is seen, this will need further hysteroscopic assessment. National guidelines are developed in order to help the management of post menopausal bleeding (British Menopausal Society, Scottish Intercollegiate Guidelines Network Royal College of Obstetrician and Gynaecologists, UK). In case of known AS, it is very difficult to explore the cervix and endometrial cavity in menopause with a hysteroscope due of the atrophy. Each individual case should be carefully assessed by a gynaecologist used to treat these conditions.

Discussion

The aim of the IUA or AS therapy is to restore an anatomical satisfactory uterine cavity that, possibly, will

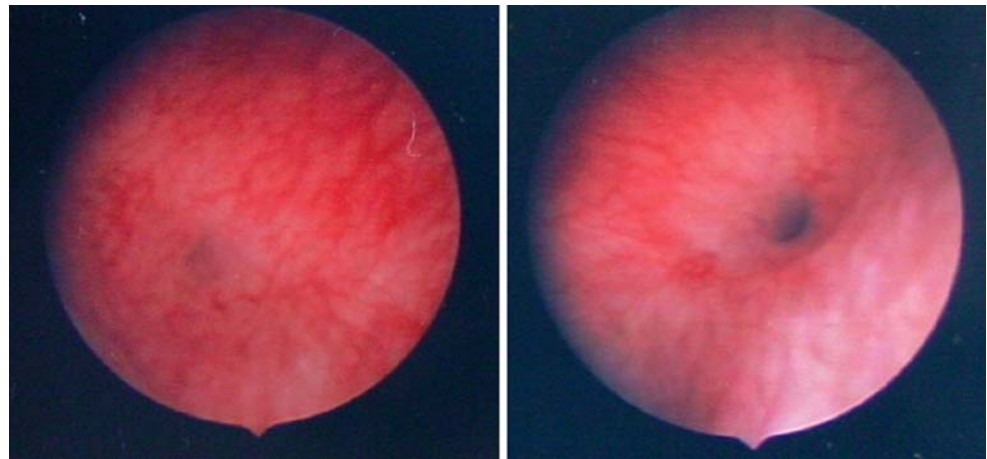
be colonised by normal endometrium. The final outcome and satisfaction of these procedures depends on the patient expectations. Successful treatment of AS is considered the return of menstrual periods. For the women with IUA-induced hypomenorrhoea, this corresponds to the return of more ‘normal’ menstrual periods in terms of quantity. Other patients expect to be relieved from cyclical pain and dysmenorrhoea. Others expect improvement of their fertility. The correlation of the visual aspect of the uterine and the endometrial function is possible but requires training [52]. It is, however, not certain that the regenerated endometrium will have a normal function even if the anatomical aspect of the cavity is restored and if there is proof of tubal patency. If the tubal ostia are not accessible, blocked or impossible to treat, in vitro fertilization is the next option for subfertile couples.

The presence of menstrual periods after surgery is a promising outcome but does not guarantee return of normal fertility. The best operative hysteroscopic techniques are not able to guarantee that the cavity will be entirely free from IUA after a single operation. Sometimes more procedures are needed. In some patients, three or four adhesiolysis attempts have to be performed until a satisfactory cavity is obtained. The more we intervene in the cavity the more destruction can be caused to the rest of the normal endometrium. It is essential that the operator preserves untouched areas that may contain normal endometrial glands in view of better postoperative colonisation of the cavity. Good knowledge of the normal hysteroscopic view of the superficial endometrium is paramount [52]. The treatment of AS and IUA should be performed by an experienced operator in order to minimise intraoperative complications and excessive adhesiolysis or trauma to the normal endometrium. The choice of the energy that will be used for the adhesiolysis plays a great role in the expected outcome. The choice depends on operator preference,



Fig. 11 View of endometrium after adhesiolysis on cervical synechias for evacuation of haematometra

Fig. 12 Hypervascularity of endometrium? Reaction to the menstrual debris



hospital available resources and overall cost effectiveness calculation.

In the 1970s and 1980s, curettage was performed without suction aspiration systems. During this period, aggressive curettage was even thought to be curative for endometrial hyperplasia or menstrual disorders. The population that was studied during this period of time (1970–1980) was treated with different instruments and operative techniques. Although the actual techniques for curettage are less traumatic, IUA or AS still is reported. There is no reported correlation between the methods of evacuation of retained products of conception in view of the appearance of IUA. Recently, AS has been reported after manual vacuum aspiration in early pregnancy failure [53].

The prophylactic use of antibiotics (AB) is a well-established precaution after curettage in the voluntary termination of pregnancy [54]. However, the type and duration of antibiotic cover is very heterogeneous in current practice. One dose of intravenous antibiotic is generally used, but it is not known if this is sufficient in order to prevent IUA. On the other hand, oral AB cover is suggested. There is no evidence-based proof that the incidence of asymptomatic endometritis is significantly decreased with the use of prophylactic AB. The oral use of AB for 5 or 7 days postoperatively has never been assessed concerning IUA formation. Some early pregnancy units (UK) do not systematically use long-term AB postoperatively in their protocols. The choice of the antibiotic is arbitrary-based, using mono-therapy or combined antibiotic cover for aerobic–anaerobic germs. The influence of the AB cover on the endometrial recolonisation is unknown.

It is difficult to assess the overall evidence on what is the best treatment for IUA or AS due to the great discrepancy of IUA classifications and its use by the surgeons, the heterogeneous patient populations and innovative ideas or treatment modalities without appropriate patient number

validation. There is significant lack of comparison between the different classifications. Even when clinical symptoms or previous obstetric history are taken into account, the lack of large population studies does not permit any definitive conclusion about which classification is better to use or even to standardise only one type of classification (consensus), which all the gynaecologists will respect. Most of the reported results were generally given by experienced operators or tertiary centres, which do not correspond to what is seen in the current general gynaecological practice. As the IUA or AS diagnosed cases are rare in number per year and per gynaecologist, collecting sufficient large numbers cases takes considerable time and it is very difficult to conclude on the prognosis only on the basis of small numbers of treated patients. This is one of the reasons why referral to appropriate minimal access surgery centres will attract larger number of patients, and this will help a better technical and more appropriate scientific approach.

Over the last 20 years, the bulk of the literature reflects on small series leaving the studies underpowered, which makes meta-analysis impossible. The misuse of the AS terminology meaning severe IUA or vice-versa makes the overall interpretation of the reported results extremely biased. Classification of the IUA degree does significantly help to evaluate the prognosis. However, there is no reported study that correlates the classification of IUA and proposed managing techniques. A classification incorporating images (visual data) may be more accurate than just the operator's subjective interpretation. The images recorded prior to and after hysteroscopic treatment may help to better classify the cases.

As hysteroscopic techniques evolved over the last 20 years, outpatient procedures are more often performed and the detection of IUA is expected to increase. A data base system is essential to record the IUA cases and review the overall treatment outcome. During outpatient hystero-

scopy, early filmy IUA are treated easily, but this fact is rarely recorded in the medical files. Maybe the overall IUA prevalence is underestimated as in light of the previous, most likely only the severe or symptomatic IUA are recorded.

The counselling of the patient is an essential part of the IUA management. The current evidence suggests that the hysteroscopic management of IUA and AS is successful and safe. Counselling the patient should include written information about the condition, the possible treatments, the possible outcome and information about website patient supportive groups.

The need for well-structured prospective studies about IUA and AS is imperative. Standardised systematic approach without biased methodology must be organised firsthand. A large multi-center European study based on strict criteria of diagnosis, classification, operative technique and outcome followed by a long-term follow-up (minimal 5 years) could answer faster most of the questions concerning IUA and AS. In fact, little is known about the pathophysiology of the endometrium concerning the significance of subclinical infections in time and their impact on gynaecological or obstetrical complications related to IUA.

Recent reports indicate more risk factors to be involved with the formation of IUA. Awareness about these factors will lead to investigate or treat high-risk women in an early stage.

For the future

We need to review the IUA or AS treatment taking into account:

- The need to develop (with validation and pragmatic clinical evaluation) a scoring system to identify women at high or low risk of IUA–AS that could be per- or posthysteroscopy-based.
- The need to identify whether there are differences in long-term menstrual and fertility outcomes between women treated with only hysteroscopic technique compared to hysteroscopy and added estrogen, IUCD or other mechanical of chemical means.
- The need to investigate the etiology and prevention of IUA especially in high-risk women.
- The need of research into the factors that may explain the variability of management options (different countries).
- The need to assess the woman's satisfaction using quality-of-life measures and health-state utilities in women following adhesiolysis with the aim of undertaking robust economic modeling assessments (to establish standards in different countries).

- The need to emphasize the role of audit in identifying areas where improvements are required and making recommendations at the regional or national level.

Conclusion

A systematic approach, audit and well-structured research are mandatory in order to establish the best treatment for the individual needs of the patient. Clinical practice is changing significantly over the last 20 years particularly with the introduction of guidelines, standards of care and, most important, the introduction of the audit as a tool to evaluate the treatment efficacy, short- and long-term outcomes. Hysteroscopic treatment seems effective and safe. The incidence of IUA or AS is not high in the general gynaecological practice. Therefore, the referral to a tertiary centre for management may help to centralise most of the cases and to have the opportunity to study more in detail the efficacy of each treatment modality.

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