How can surgery increase the success rate in ART?

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MANAGEMENT OF INTRAUTERINE SYNAECHIE?

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HISTORY

✓ 1894 – Heinrich Fritsch
First described a case of posttraumatic intrauterine adhesion.

✓ 1927 – Bass
✓ 1946 – Stamer
✓ 1948 – Joseph G. Asherman

Asherman Syndrome has been used to describe the disease ever since.

DEFINITION

✓ Intrauterine adhesions are:
  a consequence of trauma to the endometrium, producing partial or complete obliteration in the uterine cavity and/or the cervical canal.

✓ The prevalence varies both by different populations as well as by the types of investigation used for diagnosis.
  (approximately 1-5%)

Al-Inany H. Acta Obstet Gynecol Scand 2002
**Asherman syndrome—one century later**

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**The criteria for the diagnosis of Asherman syndrome:**

I. At least one of the following clinical features;
   - Amenorrhea
   - Hypomenorrhea
   - Amenorrhea, hypomenorrhea
   - Subfertility, infertility
   - Recurrent pregnancy loss
   - History of abnormal placentalation (previa, acreta...)

II. The presence of intrauterine adhesions by Hysteroscopy and/or histologically confirmed intrauterine fibrosis.

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**ETIOLOGY**

I. Trauma to a gravid uterine cavity (%66.7)
   - Curettage (postpartum, postabortion, elective)
   - Cesarean section
   - Evacuation of hydatiform mole

II. Trauma to nongravid endometrium
   - (Diagnostic curettage, myomectomy, insertion of a IUD, operative hysteroscopy...)

III. Infection (chronic or subacute endometritis)

IV. Congenital anomaly of the uterus (esp. Septate uterus)

V. Genetic predisposition

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**CLASSIFICATION**

**European Society of Gynecological Endoscopy (ESGE) 1995**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description of intrauterine adhesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Thin or filmy adhesions</td>
</tr>
<tr>
<td>II</td>
<td>Single dense adhesion</td>
</tr>
<tr>
<td>III</td>
<td>Multiple dense adhesions</td>
</tr>
<tr>
<td>IVa</td>
<td>Extensive dense adhesions involving the cervical canal and uterine cavity</td>
</tr>
<tr>
<td>IVb</td>
<td>Extensive dense adhesions involving the cervical canal and uterine cavity</td>
</tr>
<tr>
<td>V</td>
<td>Extensive adhesions involving the cervical canal and uterine cavity</td>
</tr>
</tbody>
</table>

Endoscopic surgery for gynaecologists, 1998
**SYMPTOMATOLOGY**

I. Menstrual abnormalities (%68)
II. Infertility (%43)
III. Recurrent pregnancy loss
IV. Other pregnancy complications
    ✓ Spontaneous miscarriage
    ✓ Preterm delivery
    ✓ Abnormal placental implantation
    ✓ Ectopic pregnancy
    ✓ IUGR - ?

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**CLINICAL – PATHOLOGICAL CORRELATION**

✓ The clinical features are closely associated with pathological findings in Asherman syndrome.

✓ These pathological findings are:
    ✓ The depth of fibrosis
    ✓ The location of the adhesions
    ✓ The extent of the pathologic changes

Dan Yu et al. Fertil Steril 2008

**CLINICAL – PATHOLOGICAL CORRELATION**

Clinical/pathology correlation of Asherman syndrome:
- Location of the pathology of Asherman’s syndrome
- Variable
- Obstructive amenorrhea
- Variable
- Amenorrhea and infertility
- Obstructive amenorrhea

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**DIAGNOSIS**

I. Radiological Diagnosis
- Hysterosalphingography
- Ultrasonography
- Sonohysterography
- MRI

II. Hysteroscopy

**IU Adhesions Management**

**AIM**
- Restoration of the uterine cavity
- Prevention of recurrence
- Endometrial restoration
- Maintenance of the normal cavity

**PROCEDURE**
- Adhesiolysis (H/S)
  - Lippes loop
  - High dose estrogen therapy
- Follow up by H/S or HSG after treatment

**TREATMENT**
- Expectant Management
- Dilatation & Curettage
- Hysterotomy
- Hysteroscopy
- Because of its minimally invasive nature and also because it can be performed under direct vision, "Hysteroscopy" is currently the gold standard for the treatment of intrauterine adhesions.
**HYSTEROSCOPIC ADHESIOLYSIS**

- Adhesiolysis usually begins inferiorly and can be advanced until the uterine architecture has been restored. In most cases adhesiolysis can be performed by scissors or graspers but sometimes electrosurgery is needed.

Hysteroscopic adhesiolysis is a safe and effective procedure for restoring the normal menstrual pattern and fertility.

Pabuçcu R., Fertil Steril, 1997

- Forty women with recurrent pregnancy loss or infertility resulting from intrauterine adhesions.

After hysteroscopic adhesiolysis:
- In 36 infertile cases:
  - 86% (n=30) conceived,
  - 63% (n=24) term or viable preterm delivery
- In 24 cases with recurrent pregnancy loss:
  - 71% term or viable preterm delivery

Pabuçcu R., Fertil Steril, 1997
**Hysteroscopic Adhesiolysis**

- Hysteroscopic adhesiolysis using scissors or biopsy forceps has the advantages of:
  - Avoiding complications related to energy sources,
  - Minimizing the further destruction of the endometrium,
  - Decreasing the recurrent adhesion formation.

Fedele L, Acta Eur Fertil 1986
Feng ZC, Gynaecol Endosc 1999

**Hysteroscopic Adhesiolysis**

- Hysteroscopic surgery using energy sources such as laser vaporization or electrodes provides effective and precise cutting as well as better hemostasis. But there is a possibility of further endometrial thermal damage.

Duffy S, J Obstet Gynaecol 1992
Roy F, Gynaecol Endosc 1997

- However, other authors suggest that there is no difference between the use of scissors and resectoscope. Also electrosurgery achieves better hemostasis, thus providing an improved clarity of the operative field.

De Cherney A, Obstet Gynecol 1983
Carrauch M, Human Reproduction 1994

**Reproductive outcome following hysteroscopic adhesiolysis in patients with fertility due to Asherman’s syndrome**

- 89 patients with infertility due to Asherman syndrome
- Retrospective clinical analysis
- Hysteroscopic adhesiolysis by monopolar electrode knife
- A second look office hysteroscopy was performed in all cases after 2 months

Roy K et al. Arch Gynecol Obstet, 2010
Reproductive outcome following hysteroscopic adhesiolysis in patients with fertility due to Asherman's syndrome

- 12 patients showed reformation of adhesions and needed a repeat procedure
- Conception rate 40.4 %
- Live birth rate 86.1 %
- Miscarriage rate 11.1 %
- Hysteroscopic adhesiolysis is safe and effective for restoring menstrual function and fertility.

Roy K et al. Arch Gynecol Obstet, 2010

Hysteroscopic adhesiolysis

- Hysteroscopic management of the intrauterine adhesions, especially the severe and dense ones;
  - May be technically difficult.
  - Also carries a significant risk of uterine perforation.
- Perforation usually occurs during the dilatation of the cervical canal or / and the introduction of the hysteroscope.

In order to improve the safety and efficiency of the hysteroscopic adhesiolysis, and also to minimize the risk of uterine perforation the procedure can be guided by one of the following methods:

- Laparoscopy
- Transabdominal ultrasonography
- Fluoroscopic control
- Gynecoradiologic uterine resection
PREVENTION OF RECURRENT ADHESIONS

- Because of the high rate of reformation of the adhesions (%3.1 - 23.5), esp. the severe ones (%20-62.5), prevention after surgery is essential.
- The risk is directly correlated with the type and the etiology of adhesions.

PREVENTION OF RECURRENT ADHESIONS

- Prevention of recurrent adhesions after surgery is essential for a successful treatment.
- Methods used for prevention:
  1. Second/Third look hysteroscopic adhesiolysis
  2. Barrier Methods (Sepra film, hyaluronic acid gel, amnion graft)
  3. Mechanical Methods (IUD, Lippes loop, Foley balloon)
  4. Hormone Treatment (estrogen, progesterin, GnRH analogues, danazol)
  5. Pharmacologic Agents (antibiotics, NSAID, Ca antagonists, antihistaminics)

PREVENTION OF RECURRENT ADHESIONS

1) SERIAL HYSTERO(SCOPY)

- Serial hysteroscopic adhesiolysis after primary treatment of intrauterine adhesions, is an effective method for the maintenance of the cavity as well as the prevention of recurrence.
Postoperative adhesiolysis therapy for intrauterine adhesions (Asherman’s syndrome)

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

DESIGN: Retrospective analysis of 24 patients treated with primary hysteroscopic adhesiolysis followed by hormone therapy and serial flexible office hysteroscopy.

Initial postoperative office hysteroscopies were performed within 2 weeks of the primary surgery. Subsequent hysteroscopies were performed every 1-3 weeks until minimal to no disease remained.

RESULTS:
- Improvement in menstrual flow in 95%.
- Relief of dysmenorrhea in 82% and.
- 46% of fertility patients were actively pregnant or had delivered viable infants.

PREVENTION OF RECURRENT ADHESIONS

2) BARRIER METHODS

Seprafilm, is a biodegradable membrane of chemically modified hyaluronic acid and carbosyliccellulose, was shown to be effective in reducing adhesion formation.

Limited evidence that Seprafilm was effective in preventing adhesion formation following gynecological surgery for myomectomy (Cochrane Database Syst Rev 2008, CD000475)
The role of Seprafilm bioresorbable membrane in the prevention and therapy of endometrial synechiae

- 150 patients with incomplete or missed abortion undergoing D&C
- Seprafilm treatment n = 50, Control group n = 100
- Synechiae was evaluated with HSG
- More than 50% of the patients where Seprafilm was used were adhesion free
- Intrauterine insertion of Seprafilm is safe and prevents the appearance of endocervical adhesions.
- Placement of Seprafilm; into the both cervical canal and endometrial cavity after suction evacuation or curettage for incomplete, missed and recurrent abortion, effectively prevents adhesion formation


Prevention of recurrent adhesions

2) BARRIER METHODS

- Auto-cross linked hyaluronic acid (ACP) gel

- Hyaluronic acid is a natural component of the extracellular matrix and has been suggested as a possible adhesion barrier.

Effectiveness of auto-cross-linked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic adhesiolysis: a prospective, randomized, controlled study

- 92 patients with irregular menses and intrauterine adhesions
- Prospective randomized study
- Group A: H/S plus ACP gel n=43
- Group B: H/S n=41
- ACP gel reduces the development of IU adhesions.

Acunzo G et al. Hum Reprod 2003

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A (ACP gel) (n = 43)</th>
<th>Group B (control) (n = 41)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years ± SD)</td>
<td>36.8 ± 11</td>
<td>36.7 ± 24</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg) ± SD</td>
<td>61.9 ± 16</td>
<td>61.2 ± 16</td>
<td>NS</td>
</tr>
<tr>
<td>Under (cm × cm) ± SD</td>
<td>6.9 ± 1.2</td>
<td>6.4 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>FSH</td>
<td>1.3 ± 0.2</td>
<td>1.2 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>Number of sterile patients</td>
<td>16</td>
<td>30</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant.
Effectiveness of auto-crosslinked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic surgery: a prospective, randomized, controlled study

Auto-cross linked hyaluronic acid (ACP) gel

After hysteroscopic adhesiolysis intracavitary ACP gel application, effectively prevents postoperative adhesion formation.

Interest of auto-cross-linked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic surgery: a case control study

- 54 cases with IU lesions
- Group A n=30 H/S plus hyaluronic acid gel
- Group B n=24 H/S
- No difference in IU adhesion formation.
**PREVENTION OF RECURRENT ADHESIONS**

2) **BARRIER METHODS**

- **Amnion Graft**
  - Fresh amnion graft draped over an inflated Foley catheter balloon

Amnion graft following hysteroscopic lysis of intrauterine adhesions

- Hysteroscopic adhesiolysis was followed by introduction of fresh amnion graft draped over an inflated Foley catheter balloon in 25 patients.
- Repeat hysteroscopy showed further adhesion formation in 48% but all these were minimal.
- Long-term data are not available

*Amer MI et al, J Obstet Gynecol Res, 2006*

Human amnion as a temporary biologic barrier after hysteroscopic lysis of severe intrauterine adhesions, pilot study

- 45 patients with severe intrauterine adhesions
- Group 1 n=15 intrauterine balloon
- Group 2 n=15 fresh amniotic graft
- Group 3 n=15 dried amnion graft for 2 weeks
- H/S 2-4 months postop.
- Significant improvement in adhesion graft vs IU balloon. Greater improvement with fresh amnion

*Amer et al., 2010, J Min Inv Gynecol*
2) BARRIER METHODS

Amnion graft is a promising adjunctive procedure for decreasing recurrence of adhesions and encouraging endometrial regeneration.

PREVENTION OF RECURRENT ADHESIONS

3) MECHANICAL METHODS

✓ Some studies reported that the application of a 8 – 10 F Foley catheter into the uterine cavity with an inflated balloon for several days after adhesiolysis may prevent recurrence.

Amer MI et al. MEFS J 2005

✓ In a comparative study, after lysis of adhesions either a 10 F Foley catheter balloon, inflated with 3,5 ml of saline was left in the uterine cavity for 10 days or Lippes loop was placed for 3 months.

✓ Foley catheter resulted in a greater proportion of women achieving normal menses(81% vs 63%), higher conception rates (34% vs 23%) and a reduced need for reoperation.

PREVENTION OF RECURRENT ADHESIONS

3) MECHANICAL METHODS

- For many years, the placement of an IUD into the uterine cavity for 3 months has been considered the standard method of maintaining the uterine cavity after surgery.
- However, the copper-bearing IUDs might induce an excessive inflammatory reaction and T-shaped coils may have a too small surface area to maintain the uterine cavity.
- Some authors suggested that larger inert devices such as Lippes-loop is effective in the prevention of recurrent adhesions.

Pabuccu et al., Fertil Steril 2008

Efficiency and pregnancy outcome of serial intrauterine device–guided hysteroscopic adhesiolysis of intrauterine synechiae

- Prospective, randomized trial to highlight the efficiency of Lippes loop guidance during hysteroscopic adhesiolysis for severe adhesions.
- 71 subfertile patients with severe intrauterine adhesions.
- Patients were randomized into 2 groups;
  - Group 1: Just after hysteroscopic adhesiolysis, IUD was inserted and 1 week later a second look H/S was performed for further lysis by the guidance of IUD. (n=36)
  - Group 2: Just after hysteroscopic adhesiolysis, IUD was inserted and the patients were given estrogen-progesterone for 2 months (n=35)

Pabuccu et al., Fertil Steril 2008

An IUD-guided therapeutic approach simplifies hysteroscopic adhesiolysis for severe intrauterine adhesions. The Lippes loop IUD probably enlarges the cavity and creates bits of endometrium, which simplifies the procedure for adhesiolysis.

<table>
<thead>
<tr>
<th>Adhesion formation results</th>
<th>Group 1 (36)</th>
<th>Group 2 (35)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One wk after</td>
<td>Two wk after</td>
</tr>
<tr>
<td></td>
<td>hysteroscopy</td>
<td>hysteroscopy</td>
</tr>
<tr>
<td>Nodules</td>
<td>8 (13.3)</td>
<td>33 (91.7)</td>
</tr>
<tr>
<td>Folds</td>
<td>11 (19.5)</td>
<td>12 (32.4)</td>
</tr>
<tr>
<td>Residues</td>
<td>3 (5.2)</td>
<td>1 (2.6)</td>
</tr>
</tbody>
</table>

Pabuccu et al., Fertil Steril 2008
**PREVENTION OF RECURRENT ADHESIONS**

4) **HORMONE TREATMENT**

- Estrogen-progestin therapy significantly increases endometrial thickness and volume, but there is no objective evidence based on randomized, controlled trials to confirm the efficacy of hormone treatment on the reduction of reformation of intrauterine adhesions.

**CONCLUSION**

- "HYSTEROSCOPY" is the gold standard for diagnosis and treatment of intrauterine adhesions.

- Prevention of recurrent adhesions after surgery is essential for a successful treatment.

- There is still no single modality proven to be unequivocally effective in preventing postoperative adhesion formation after hysteroscopic surgery.