TePA-study (Tertiary Prevention of morbus Asherman-study);Evaluation of placement of hyaluronic acid (hyalobarier ® Gel Endo) and placement of a intrauterine device without cu or hormones to maintain separation of the cavity and mechanically to prevent spontaneous recurrence of adhesions.

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Does the installation hyaluronic acid (hyalobarier ® Gel Endo), in patients with M. Asherman reduces or prevents the incidence and severity (ESGE score/classification) of spontaneous recurrence of adhesion better then the IUD without Cu or hormones...

Ethical review	Approved WMO
Status	Pending
Health condition type	Uterine, pelvic and broad ligament disorders
Study type	Interventional

Summary

ID

NL-OMON43266

Source
ToetsingOnline

Brief title
TePA-study (Tertiary Prevention of morbus Asherman-study)

Condition

- Uterine, pelvic and broad ligament disorders

Synonym
Asherman

Research involving
Human

Sponsors and support

Primary sponsor: Spaarne Ziekenhuis
Source(s) of monetary or material Support: WOGOS

Intervention

Keyword: Adhesiolysis, Asherman, hyaluronic acid, Hysteroscopy

Outcome measures

Primary outcome

Incidence and severity of spontaneous recurrence of adhesions at 8-10 week

second look hysteroscopy

Secondary outcome

We aim to answer the following secondary questions which strategy of prevention

of spontaneous recurrence :

* restores the normal menstrual blood flow better on shorter (3months) and

long-term (6months and 1 year) assessed with a *Pictorial Blood Loss

Assement* (PBAC) (Appendix4).

* Has the best the pregnancy rate. This the hazard ratio for any ongoing

pregnancy (in those patients willingly to conceive) after one year follow-up.

During a follow up of 1 year the number and time to conceive will be recorded.

The clinical as well as the ongoing pregnancies (defined as intra-uterine heart

activity at 12 weeks gestation) and the course of the pregnancies will be recorded.

* Needs the highest number of re-interventions (hysteroscopic adhesiolysis in the OR or outpatient clinic or adhesiolysis without hysteroscopy (dilatation) in outpatient clinic setting) during one year per patient will be closely monitored and recorded

* Has the highest complications related to gel or IUD or any side-effect, such as intra uterine infection and discomfort of the patient.

Study description

Background summary

Recognition that organic intrauterine adhesions can lead to secondary amenorrhea has been demonstrated since the end of the 19th century, although not until 1948, when Joseph Asherman described the eponymous condition in 29 patients, did the syndrome became popularized and treatment described. Asherman*s original description related to post pregnancy intrauterine adhesions in all cases, and such adhesions remain the commonest cause of this syndrome. Asherman expanded his original thoughts, and related endometrial trauma and adhesion formation to menstrual disturbance, cyclical pelvic pain, and sub fertility including recurrent pregnancy loss. Important in his description was that the adhesions seemed to have an inherent effect on the endometrium, causing it to be inactive.
Asherman syndrome is a condition of uterine distortion resulting in amenorrhea or hypomenorrhea, infertility and recurrent pregnancy loss. The re-adhesion rate is high after (20%) surgical intervention. The prevalence of M. Asherman varies widely depending on the trauma caused to the uterus. The true incidence of this condition is difficult to determine, ranging from 1.5% of patients referred for fertility testing up to 40% of women following secondary removal of placental tissue or repeat curettage after a missed abortion .Recurrent miscarriage is often associated with intrauterine adhesions, with adhesions reported in 5% to 39% of women. The risk of developing intrauterine adhesions

postpartum is high, affecting 21.5% to 40.0% of women requiring uterine instrumentation. Postpartum hemorrhage is a risk factor for intrauterine adhesions, with an early report noting an incidence of intrauterine adhesions of 9%. Surgical treatment of a silent miscarriage (missed abortion) has been reported to lead to 31% of intrauterine adhesions compared to an incomplete miscarriage, in which only about 6.4% of women are likely to develop intrauterine adhesions. Trauma to the non pregnant uterus can also cause intrauterine adhesions, the risk is lower, with rates of intrauterine adhesions estimated to be 1.6% after diagnostic curettage, 1.3% after abdominal myomectomy, 0.5% after cervical biopsy or polypectomy, and 0.2% after insertion of an intrauterine device (IUD).
There is almost universal support that surgical treatment is the criterion standard in management of Asherman syndrome, and there is no role for medical treatments. There is no consensus as to the optimal technique of division of adhesions. The most used technique is according to the methods described by Broome and Vancaillie in 1999 .
A number of strategies have been proposed to reduce the recurrence of adhesions after surgery. Insertion of an IUD provides a physical barrier between the uterine walls, separating the endometrial layers after lysis of intrauterine adhesions . Several studies have also recently examined the application of hyaluronic acid gel into the uterine cavity after adhesiolysis. There appears to be some evidence that the hyaluronic acid gel may be of benefit in reducing intra-uterine adhesions . One cohort study compared the efficacy of three adjuvant measures (IUD, balloon and gel), the gel appeared to be the least effective . A randomized controlled trial was never performed to study this effect.

In this randomized controlled trial a comparison is made of the efficacy of the placement of the intrauterine device without Cu or hormones versus hyaluronic acid (hyalobarier ® Gel Endo) preventing adhesion reformation after adhesiolysis.

Study objective

Does the installation hyaluronic acid (hyalobarier ® Gel Endo), in patients with M. Asherman reduces or prevents the incidence and severity (ESGE score/classification) of spontaneous recurrence of adhesion better then the IUD without Cu or hormones (Flexie T) Presence and extent of adhesions will be evaluated by second look hysteroscopy between 8-10 weeks after the initial procedure, using the ESGE classification

Study design

Singlecenter prospective single blind randomised controlled trial.

Intervention

The same hysteroscopic adhesion resection will be performed on all patients, and then they will be randomly allocated to two groups.
Intervention Group: installation of gel immediately after surgery (hyalobarier ® Gel Endo)
Control Group: fitting of Cu-IUD (Multiload or Flexi-T) and will be removed 2 week prior to the second look hysteroscopy
A second look hysteroscopy will be carried out 8-10 weeks after the initial operation.

Study burden and risks

A hysteroscopy for identification of adhesions and their extent will be performed 1months after the initial operation. A pregnancy test will be performed before the examination; if positive the examination will not be performed.

The gynaecologist who will perform the second look hysteroscopy at 8-10 will be blinded for which group the patient was allocated to.

The severity and extent will be classified according to the European Society of Gynecological Endoscopy classification of IUAs (1995 version). (Appendix 3).

The menstrual blood flow will be quantified with a pictorial blood loss assessment chart (PBAC). (Appendix 4) The chart will be evaluated at the 3 months visit. Patients will be asked to fill in the chart with during the last menstrual blood loss period they have before the 3 month visit.

After 6 months they will be asked to fill in a PBAC as well. The patients will be addressed by telephone or email.

After 1 year patients will be addressed by phone or email. During a follow up of 1 year the number and time to conceive will be recorded. The clinical as well as the ongoing pregnancies (defined as intra-uterine heart activity * 12 weeks gestation) and the course of the pregnancies will be recorded.
The number of patient requiring hysteroscopic treatment for adhesions will also be recorded.
The number of patients requiring cervical dilation in an outpatient clinic setting will also be recorded

Contacts

Public
Spaarne Ziekenhuis

Spaarnepoort 1
Hoofddorp 2130 AT
NL
Scientific
Spaarne Ziekenhuis

Spaarnepoort 1
Hoofddorp 2130 AT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Consented patients with M. Asherman who had a successful hysteroscopic adhesiolysis, defined as a restore of the normal uterine cavity, are eligible for inclusion. Patients with M. Asherman should be defined as patients with any diminishing of blood flow (secondary amenorrhoea or secondary hypomenorrhoe) after trauma, hypoxia or infection to the uterine cavity due to pregnancy related surgical procedure with the presence of intrauterine adhesions with a previous history of normal menstrual blood flow.

Exclusion criteria

- Patients with a suspected M. Asherman due to tuberculosis or schitsosomiasis.
- Patients with an uncorrected anovulation, amenorrhoe or oligomenorrhoe previous to the M. Asherman syndrome
- Patients with suspected M. Asherman due to hysteroscopic surgery with the use of electrocoagulation (used in fibroid or polyp surgery)
- Patients with congenital uterine anomalies
- Patients with contraindications for a surgical adhesiolysis
- Patients who do not master the Dutch or English language.

- Patients who are younger than 18 years of age or mentally incompetent.
- Patients with contraindications for Cu_IUD gel(hyalobarier ® Gel Endo)
- Patients who use hormonal suppletion

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2016
Enrollment:	110
Type:	Anticipated

Ethics review

Approved WMO

Date:	23-06-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL57921.094.16