Comparative, controlled trial of treatment of minor uterine cavity abnormalities diagnosed by office hysteroscopy screening in women indicated for IVF.

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To evaluate the impact of treatment of undetected, asymptomatic, predefined uterine abnormalities on the success of IVF treatment

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cervix disorders (excl infections and inflammations)
Study type	Interventional

Summary

ID

NL-OMON30448

Source
ToetsingOnline

Brief title
Treatment Efficacy of uterine Abnormalities (TEA) trial

Condition

- Cervix disorders (excl infections and inflammations)

Synonym
uterine cavity abnormalities

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Hysterosopy, In vitro fertilisation, Uterien cavity

Outcome measures

Primary outcome

The main study parameters are:

Uterine cavity condition

1. Normal cavity (including uterus arcuatus), or

2. Predefined Cavitary Abnormality:

- Partial septum (<50% of the cavity)

- Submucosal Fibroid: grade 0 (see classification)

- Endometrial Polyps taking less than 50% of the cavity

- Moderate adhesions:
- Chronic or acute endometritis (Diagnosed by the pathologist)

The main study endpoints are:

• Cumulative Ongoing pregnancy rate achieved in a one year IVF/ICSI treatment

period

• Cumulative implantation rate achieved within a one year IVF/ICSI treatment

period

Secondary outcome

Not applicable

Study description

Background summary

Despite advances in IVF procedures and the transfer of embryos of high morphological quality, pregnancy rates from IVF remain around 30% per embryo transfer procedure. Failure of transferred embryos to implant remains the most important limiting factor determining in vitro fertilization (IVF) or intra cytoplasmic sperm injection (ICSI) success rates. If progress is to be made in improving implantation rates, a greater understanding of the factors which determine successful implantation is required. Recurrent implantation failure after IVF may be due to an endometrial, an embryo problem or both
Although the influence of uterine cavity abnormalities on outcome of infertility treatment is largely unknown, treatment of these abnormalities has been advocated on a wide scale without any evidence. Prospective and randomized studies evaluating the consequences of predefined uterine cavity deformities (septum arcuatus, bicornis) or intra cavitary abnormalities (submucosal myomas, endometrial polyps, endometritis) on fertility outcome are very few. Therefore, the influence of treatment of these abnormalities on fertility outcome is even less well known. The current literature describes an incidence of unexpected uterine abnormalities observed by hysteroscopy evaluation of ~ 40% in cases with normal TVS and no clinical signs. In cases treated for the predefined abnormality the increase in cumulative ongoing pregnancy rate after two consecutive cycles of IVF/ICSI is estimated to be 15% (25 versus 40%)

Study objective

To evaluate the impact of treatment of undetected, asymptomatic, predefined uterine abnormalities on the success of IVF treatment

Study design

Patients scheduled for a first IVF/ICSI treatment at the VUB/Utrecht/Rotterdam undergo a standard office hysteroscopy in the follicular phase of a cycle 1-3 months before starting the IVF/ICSI treatment. In the case of finding a predefined intra uterine abnormality randomization will be carried out after informed consent for endoscopy treatment versus no treatment. Shortly after the hysteroscopy screening and procedure IVF/ICSI treatment is initiated and outcome during a one year treatment period recorded.
Follow up of the study group will comprise the period of one year subsequent to the initiation of the first IVF/ICSI treatment, in which any treatment cycle and any pregnancy occurring will be recorded and defined.

Intervention

Office Hysteroscopy procedure
Hysteroscopy will be performed under supervision of the same investigating team (FB and MK) on an outpatient basis under paracervical block using in total 10 ml Xylocaine 1%. Hysteroscopy will be done with the use of a 5-mm outer-diameter continuous flow hysteroscope with 5 French working channel and a 30o direction of view. The uterine cavity will be distended with the use of physiologic saline infusion at a maximum pressure of 150 mmHg. The endocervical canal, uterine cavity, tubal orifices and endometrium will be inspected methodically and findings recorded into a standardised form. A sample of the endometrium will be obtained for histologic examination by a gentle biopsy with the Pipelle biopsy canulla. Pictures will be recorded and filed for each patient with predefined abnormalities. Therapeutic hysteroscopy will be performed in the same hysteroscopy session if the patient is randomized as such.

Intervention:
- Septum resection with Resectoscope Storz or Versapoint®.
- Polyps resection with Resectoscope Storz or Versapoint®
- Resection of the myoma with the Resectoscope Storz or Versapoint®
- Resection of the adhesions with Hysteroscopic scissors or Versapoint®
- Chronic and acute endometritis: Ofloxacinum 400mg/day orally should be used during 5 days (both partners) and after the menstruation a new biopsy should be taken to confirm the effect of the treatment. Alternative: Doxycline 100mg: 2x100mg on day one, followed by 100mg/day during 8 days.

Controlled ovarian hyperstimulation for IVF/ICSI
Rec-FSH or HMG, long (day 21) agonist protocol (Buserelin or Triptorelin) or day 6 GnRH antagonist protocol (Ganirelix / Cetrorelix 0.25mg/d) will be used. Final oocyte maturation by administration of 10.000 IU of HCG (Pregnyl®) as soon as >= 3 follicles of >= 17 mm are present. Oocyte retrieval will be carried out 36 hours after HCG administration. IVF/ICSI. ETd3/d5. Luteal phase supplementation: 600mg natural micronised progesterone in three separate doses (Utrogestan® / Progestan® 100mg 3x2/day) starting one day after oocyte retrieval and continued until 7 weeks of gestation if pregnancy is achieved.

Study burden and risks

Burden
Patients indicated for IVF/ICSI undergo a routine hysteroscopic screening. In the case of any predefined intra cavitary they will be randomised during the procedure to either undergo or not undergo a surgical correction of the abnormality. This will increase the time length of the procedure by a factor 2 to 3. In case inflammation of the endometrium will be diagnosed additional treatment with antibiotics for 2 weeks will be prescribed.

Risks
Hysteroscopy procedures introduce a risk of procedure related complications,

like cervical or uterine perforation, intra-uterine infection or bleeding. Also risk of cardiovascular compromise due to the use of local anaesthetics and allergic reaction to antibiotic treatment are included. Based on existing literature these risks are very limited (Sutton, 2006) and estimated to be below 0,1%.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Normal Transvaginal Ultrasound
- No prior hysteroscopy
- Age <= 36 years
- Regular menstrual cycle
- Single Embryo Transfer

- BMI between 18 and 29
- Presence of both ovaries
- Primary or secondary infertility
- Women indicated for a first IVF/ICSI treatment

Exclusion criteria

- Recurrent miscarriage
- Prior hysteroscopic treatments
- Endometriosis >= AFS Stage III
- Meno-metrorrhagia (defined as any intermenstrual loss of blood)
- Submucosal/Intracavitary Fibroids taking more than 50% of the cavity
- Hydrosalpinx
- FSH/ LH > 12 IU/L on day 3
- Polyps taking more than 50 % of the cavity

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-06-2007
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	19-02-2007

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL13183.041.06