Tubal flushing with oil-based contrast during HSG in subfertile women: Is early flushing effective and cost-effective as compared to delayed flushing?

Published: 23-07-2019
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The aim of this study is to determine whether direct tubal flushing with oil-based contrast at HSG incorporated in the fertility work-up results in 10% more ongoing pregnancies and a shorter time to pregnancy, which will therefore be effective and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Ovarian and fallopian tube disorders
Study type	Interventional

Summary

ID

NL-OMON52895

Source
ToetsingOnline

Brief title
H2Oil-timing study

Condition

- Ovarian and fallopian tube disorders

Synonym
testing whether the fallopian tubes are open, Tubal patency testing

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMw,Guerbet

Intervention

Keyword: - Hysterosalpingography, - Oil-based contrast, - Ongoing pregnancy, - Time-to-pregnancy

Outcome measures

Primary outcome

Primary outcome is time to life birth within 6 and 12 months after randomization. Time to live birth within 6 months after randomization provides us information about the comparison on HSG with oil-based contrast performed during fertility work-up compared to no HSG. Time to live birth within 12 months after randomization provides information on the comparison of HSG with oil-based contract during fertility work-up versus 6 months after completing fertility work-up. Our hypothesis is that tubal flushing at HSG with oil-based contrast incorporated in the fertility work-up will result in 10% more ongoing pregnancies and a shorter time to pregnancy, and thus reducing the need for ART and reducing costs.

Secondary outcome

- Life birth
- Clinical pregnancy
- Ongoing pregnancy
- Miscarriage
- Ectopic pregnancy
- Multiple pregnancy
- Complications following HSG (infection, intravastion)

- Pregnancy outcomes (f.e. birth weight)

- Pregnancy complications

- Stillbirth

- Thyroid function of the woman (before and 1 month after HSG)

- Neonatal outcomes

- Additional fertility treatments (Intra-uterine insemination, IVF, IVF/ICSI)

- Direct and indirect costs within 12 months after randomization

- Thyroid function of neonate (determined by heelprick by RIVM)

- Level of pain and anxiety during HSG

Study description

Background summary

Staying childless, due to the inability to conceive, is one of life*s great misfortunes. Infertility, defined as the inability to conceive within 1 year of unprotected intercourse, affects 1 out of 6 couples trying to get pregnant. The causes of infertility can be classified as anovulation, poor sperm quality and tubal pathology, with unexplained infertility as a large fourth segment.
Fertility work-up generally includes an assessment of the (ovulatory) cycle, a semen analysis and an tubal patency test. This evaluation of the tubes can be done by several different tests, including a diagnostic laparoscopy, a hysterosalphingo-foam sonography or a hysterosalpingography (HSG). An HSG is the most widely used outpatient method for tubal patency testing during the fertility work-up.
Although HSG was introduced as a diagnostic test, it has been hypothesized for decades that tubal flushing at HSG in general, and specifically with oil contrast, directly increases pregnancy rates. However, the evidence for this fertility enhancement effect was lacking due to limited power of available studies. Therefore, our group completed a large randomized clinical trial (H2Oil study) comparing oil contrast or water contrast in infertile women undergoing HSG. This landmark study showed that tubal flushing with oil contrast resulted in a higher 6-month ongoing pregnancy rates than tubal flushing with water contrast (39.7% versus 29.1%) (RR 1.37, 95%CI 1.16-1.61) (Dreyer et al., 2017). The subsequent live-birth rate was also significantly higher.

Our findings have fueled the debate about the timing of HSG with oil-based contrast in the basic fertility work-up. One issue is that in our H2Oil trial the median duration of infertility of participating couples was 20 months. It is, however, unclear whether direct tubal flushing (preferably at 12 months unfulfilled child wish) with oil contrast work-up is beneficial. Direct tubal flushing with oil contrast as part of the fertility work-up might result in a shorter time to pregnancy compared to delayed tubal flushing 6 months after completion of fertility work-up.

Study objective

The aim of this study is to determine whether direct tubal flushing with oil-based contrast at HSG incorporated in the fertility work-up results in 10% more ongoing pregnancies and a shorter time to pregnancy, which will therefore be effective and cost-effective compared to delayed tubal flushing 6 months after fertility work-up is completed in women at low risk for tubal pathology.

Study design

We plan a multicentre randomized controlled trial with an economic analysis alongside it. Infertile women at low risk for tubal pathology will be randomized to direct tubal flushing with oil-based contrast incorporated in the fertility work-up or delayed tubal flushing 6 months after fertility work-up is completed.

Intervention

Direct tubal flushing with oil-based contrast as part of the fertility work-up compared to delayed tubal flushing 6 months after the fertility work-up is completed.

Study burden and risks

As we compare strategies (tubal flushing at HSG with oil-based contrast incorporated in the fertility work-up versus 6 months after completion of fertility work-up) that are already applied in current practice, no additional risks or burdens are expected from the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Women between 18-39 years of age
- Spontaneous menstrual cycle
- Perceived low risk for tubal pathology
- Undergoing fertility work-up with an indication for tubal patency testing

Exclusion criteria

- Women with known endocrine disorders (e.g. the polycystic ovary syndrome, diabetes, hyperthyroidism and hyperprolactinemia, except for well managed hypothyroidism (TSH 0.3-2.5mIU/l))
- Ovulation disorders defined as less than eight menstrual cycles per year
- Iodine allergy
- Male subfertility defined as a post-wash total motile sperm count < 1 x10^6 spermatozoa/ml
- Not willing or able to sign the consent form

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-08-2019
Enrollment:	354
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lipiodol
Generic name:	Ethyl esters of iodized fatty acids of poppy seed oil
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-07-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	14-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	04-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2022
Application type:	Amendment
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

ID: 23111
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-004153-24-NL
CCMO	NL62838.029.19
Other	NTR NL7926
OMON	NL-OMON23111