A randomised controlled trial comparing in vitro maturation of oocytes with in vitro fertilisation in women with an increased risk of ovarian hyperstimulation syndrome.

Published: 03-12-2009
Last updated: 04-05-2024

Primary objective: To evaluate the cumulative live birth rate for two treatment strategies: 2 IVM/ICSI cycles versus 1 COH/IVF or COH/ICSI cycle.Secondary Objectives: To evaluate the health and development of IVM/ICSI children versus COH/IVF/ICSI...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sexual function and fertility disorders
Study type	Interventional

Summary

ID

NL-OMON33044

Source
ToetsingOnline

Brief title
IVM

Condition

- Sexual function and fertility disorders

Synonym
subfertility, unvoluntary childlessness

Research involving
Human

Sponsors and support

Primary sponsor: Jeroen Bosch Ziekenhuis
Source(s) of monetary or material Support: aanvraag ZonNw wordt gedaan

Intervention

Keyword: in vitro fertilisation, in vitro maturation, ovarian hyperstimulation syndrome, polycystic ovary syndrome

Outcome measures

Primary outcome

Cumulative live birth rate after IVM/ICSI or COH/IVF/ICSI strategy.

Secondary outcome

- Health and development of IVM/ICSI children versus COH/IVF/ICSI children in a

5 years* follow up program

- Number and nature of adverse events during or following the two treatment

strategies, specifically including OHSS and multiple pregnancies.

- Direct and indirect costs of the two treatment strategies.

- Patients* quality of life scores as derived from validated questionnaires.

Study description

Background summary

Current ART requires COH to increase the number of oocytes. COH can lead to OHSS. In IVM immature oocytes are harvested from the ovaries without COH and matured in vitro in approximately 30 hours. These in vitro matured oocytes can be fertilised by IVF or ICSI. The first IVM-pregnancy was reported in 1991. It is estimated that since then over 1100 IVM children have been born worldwide. In recent years the IVM technique has become increasingly effective. In observational studies the delivery rate of an IVM cycle was 10-15%. Due to the absence of COH IVM has a potential benefit for patients with an increased risk of developing OHSS, such as PCOS-patients. These potential benefits extend to

patient friendliness and reduced costs.

Study objective

Primary objective: To evaluate the cumulative live birth rate for two treatment strategies: 2 IVM/ICSI cycles versus 1 COH/IVF or COH/ICSI cycle.
Secondary Objectives: To evaluate the health and development of IVM/ICSI children versus COH/IVF/ICSI children in 5 years* follow up program. To evaluate the number and nature of adverse events during or following the two treatment strategies. To evaluate the direct and indirect costs of the two treatment strategies. To evaluate patients* quality of life during and after the two treatment strategies.

Study design

Multicentre randomised clinical trial in 400 couples. The trial will be preceded by a pilot study of 50 non-randomised IVM cycles for implementation of the technique.

Intervention

2 IVM/ICSI cycles or 1 COH/IVF or COH/ICSI cycle.

Study burden and risks

Advantages of IVM
The main advantage of IVM is that a number of oocytes can be retrieved without COH. This makes it a more patient friendly procedure. The risk of OHSS is also abolished and the costs per cycle are lower in IVM/ICSI than in COHIVF or COH/ICSI. Severe OHSS occurs in 2% of IVF cycles, PCOS patients especially are at risk. Severe OHSS can entail ascites, pleural effusion, dyspnoea, organ failure and venous thrombosis or lung embolism. Also death from OHSS has occurred. OHSS is treated by hospital admittance, intravenous fluids, anticlotting therapy and draining of ascites (NVOG-guideline no. 11).

Disadvantages of IVM
The oocyte retrieval in IVM is technically more difficult and possibly more painful. The efficiency per cycle is lower in IVM/ICSI than in COH/IVF of COH/ICSI. IVM is more laborious for the IVF lab. The safety of IVM for the offspring is still subject to debate.

Risks of IVM for the woman
Oocyte retrieval in IVM, as in IVF, has the risks of bleeding and infection. Possibly these risks are larger in IVM as the retrieval is technically more demanding and takes more time. Although it can be expected that IVM oocyte retrieval is more painful, in a study on perception of pain, pain was less than

expected and acceptable to patients (Hildebrandt 2001). There are no published studies in which IVM and IVF oocyte retrievals were compared directly.

Risks of IVM for the child
IVM is possibly associated with an increased risk for congenital abnormalities and developmental disorders. Theoretically, such risks can arise from the use of immature oocytes or disturbance of genetic imprinting during in vitro maturation procedures. In some domestic animals IVM was associated with *large offspring syndrome*. However, further animal studies showed that this syndrome could not be attributed to IVM exclusively. Also super ovulation, prolonged incubation time and the IVF procedure can be pointed out as risk factors for the *large offspring syndrome* (Van Wagtendonk-de Leeuw et al., 2000). *Large offspring syndrome* in humans has not been documented thus far. In the mouse model, the long terms health effects of IVM on the offspring was studied and appeared to be minimal apart from slight changes in pulse rate and cardiac output (Eppig et al., 2009).
Health studies on IVM children are still limited, as summarised in the table in Attachment 1. In all, group sizes are relatively small and follow up periods short. In a single study children were monitored until the age of two years. The studies on IVM children reported birth weights in the normal range, therefore no signs of *large offspring syndrome* are present. Furthermore, the incidence of congenital abnormalities is not increased in IVM children compared to the general population.

Contacts

Public
Jeroen Bosch Ziekenhuis

Postbus 90153
5200 ME 's-Hertogenbosch
NL
Scientific
Jeroen Bosch Ziekenhuis

Postbus 90153
5200 ME 's-Hertogenbosch
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Women with PCOS according to the Rotterdam Criteria (The Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group, 2004) which not did achieve an ongoing pregnancy after ovulation induction (with clomiphene citrate or LEO and rFSH)
- Women with an IVF or ICSI indication and increased risk for developing OHSS (history of OHSS or cycle cancellation for imminent OHSS)

Exclusion criteria

- Woman or partner younger than 18 years and woman older than 38 years
- Unable to speak or read the Dutch language
- Medical contraindication for pregnancy or childbirth
- Positive serology for Hepatitis B, C or HIV (conform: Standpunt inzake screening op infectieziekten bij kunstmatig geassisteerde voortplanting, www.embryologen.nl).
- Diminished ovarian reserve: early follicular serum FSH > 10 IU/l and/or poor response during earlier COH/IVF or COH/ICSI with ³ 150 IU rFSH/day (definition poor response: cycle cancellation in growth of < 4 follicles or < 3 oocytes after oocyte retrieval) (Bancsi 2002).
- Persisting ovarian cysts > 30 mm diameter.

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:	Recruitment stopped
Start date (anticipated):	01-03-2010
Enrollment:	450
Type:	Actual

Ethics review

Approved WMO Date:	03-12-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-05-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved Date:	09-08-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved Date:	03-01-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	NL29051.000.09