Whole genome sequencing of children born after fertilization with ICSI using testicular sperm

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON37802

Source
ToetsingOnline

Brief title
Genome sequencing in TESE children

Condition

- Other condition
- Congenital and hereditary disorders NEC

Synonym
genetic anomalies

Health condition

observationele studie van nakomelingen van onvruchtbare mannen

Research involving
Human

Sponsors and support

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

Intervention

Keyword: follow up, genetic anomalies, genome sequencing, testicualr sperm

Outcome measures

Primary outcome

The number and type of de novo mutations found in the study group (TESE-ICSI

children).

Secondary outcome

Not applicable

Study description

Background summary

Azoospermia is one of the most severe forms of male infertility, no sperm is found in the ejaculate. Azoospermia is observed in about 5-10% of infertile couples, the origin is a spermatogenetic abnormality where sperm maturation and production is affected. In about half of the males with azoospermia, sperm can be found in the testis. By taking a testicular biopsy (testicular sperm extraction, TESE), sperm can be found and isolated to be used for intracytoplasmic sperm injection (ICSI). After fertilization of the oocytes with this testicular sperm, the best embryo*s (maximally 2) are transferred to the female partner (fresh embryo transfer, ET) or embryo's are cryopreserved for a later transfer (cryo- ET). The pregnancy rates with TESE-ICSI embryo*s are comparable to the pregnancy rates with standard IVF procedures using ejaculated sperm.
ICSI-TESE has been introduced in 1993 (Brussels) and is the treatment of choice for male fertility treatment in case of non-obstructive azoospermia. In the Netherlands, TESE was not allowed until 2007, when the CCMO allowed it again under a strict research protocol (NL12408.000.06). The available literature concerning the follow up of the children born from TESE-ICSI indicates that the risk of genetic anomalies or congenital malformations does not differ from children born after ICSI or IVF with ejaculated sperm. In our own data

including ICSI children and PESA-ICSI children (from epididymal sperm), we found no differences between both groups (see doctoral thesis dr. G. Woldringh, and Woldringh G.H., Hum Reprod Update 2010;16(1):12-9, Woldringh G.H., Hum Reprod 2011;26(7):1759-67). In a pilot study carried out by the same researcher, a higher number of *de novo copy number changes* (CNV) were found in the PESA-ICSI- children, however no characteristic fenotype could be attributed to them, concluding that changes found in the genome do not always have a (directly visible) clinical translation (Woldringh G.H. Hum Reprod 2009;24,233-240). With the recent introduction of Next Generation sequencing, a powerful tool for clinical research into (un)known (pathological) mutations, at the department of Human Genetics of the Radboud University Nijmegen Medical Centre. It is now possible to test the complete human exome in just one test. Taking into account the limited data available about the risk of introducing de novo mutations in TESE-children, we want to start this pilot project in order to estimate the probability of increasing DNA mutations in the offspring of non-obstructive azoospermic males.

Study objective

In this pilot study we intent to evaluate whether children born from TESE-ICSI treatment are at risk for increased de novo (pathological) mutations. This research is novel and pioneering, and never published before. We expect the outcome to be important for the use of this fertility treatment worldwide, independent of the outcome (either reassuring or not)

Study design

Observational study into the existence of de novo mutations in TESE-ICSI children born from a non-obstructive azoospermic father.

Study burden and risks

The burden or risk for the probands in this study (children and parents) is considered minimal. Patients will undergo a vena puncture once (at the local hospital/ family doctor or at the department of Human Genetics). The reason why children are involved in this study is that the TESE-ICSI technique has been re-introduced in the Netherlands since 2007, therefore the oldest children born from this treatment are not older than 4-5 years.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Ten trios (10 children and parents) will be tested. The only inclusion criteria for this study is that children are born after fertilization with testicular sperm and ICSI from males (father) with a non obstructive azoospermia (poor spermatogenesis).

Exclusion criteria

All other children and parents that do not meet the inclusion criteria. Fathers with a known genetic anomaly will be excluded from the study. Language barrier for understanding the reason for this study.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-01-2013
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	22-10-2012
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-09-2014
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	NL38292.091.12

Study results

Date completed:	29-06-2016
Results posted:	05-03-2018
Actual enrolment:	30

First publication
29-06-2016