Improving risk assessment in consanguineous couples by means of SNP analysis

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The objective of this research is to develop a method which can identify among all consanguineous couples the ones which are at high risk.

Ethical review	Approved WMO
Status	Completed
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON32549

Source
ToetsingOnline

Brief title
risk assessment in consanguineous couples by means of SNP analysis

Condition

- Congenital and hereditary disorders NEC

Synonym
autosomal recessive disorders

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: autosomal recessive disorders, consanguinity, risk differentiation, SNP analysis

Outcome measures

Primary outcome

For every individual a genotype is formed by using the SNP's. With this information for all couples the inbreeding coefficient is estimated. The estimates of inbreeding coefficient will be used as an outcome variable in the case-controle study. The expected outcome of these analyses is that the actual degree of relatedness (i.e. estimated from genotype data) of the cases is highger than the degree of relatedness of the controls.

For our cohort design a logistic regression analysis will be performed with the inbreeding coefficient as independent variable. With this information an odds-ratio can be estimated for the relationship between the inbreeding coefficient and the risk of having a child with an autosomal recessive disorder.

Secondary outcome

not applicable

Study description

Background summary

It is a known fact that children of consanguineous parents have a higher risk of being affected by an autosomal recessive disorder. For children of first cousin couples, this risk is only a few percent higher than the risk for couples that are not related. This means that some couples have a significant

high risk, while the majority has no or a very limited excess risk. At this point it is not possible to dfiferentiate between couples that have a high risk, and those who have a limited or no excess risk.

Study objective

The objective of this research is to develop a method which can identify among all consanguineous couples the ones which are at high risk.

Study design

The risk of autosomal recessive diseare in the offspring of consanguineous couples is conditonal on the presence of identical alleles with pathological mutations in both parents, decending from the common ancestor. The more DNA identical by descent is shared by the parents, the higher the risk.
By means of SNP analysis the proportion of DNA shared by consanguineous parents can be estimated. This would allow us to estimate better risk figures for consanguineous parents with a desire to have children.

We will use two different approaches in this study:
The case-control design will allow us to test whether consanguineous partners with children affected by autosomal recessive diseases share more DNA, identical by descent, than consanguineous partner who are believed to be related to the same degree, but only have healthy children. For our cohort design we will contact consanguineous couples with a desire to have children. The cohort design will be used to obtain different risk figure estimates for the different proportions of DNA shared in consanguineous couples.

Study burden and risks

Given the nature of this research - obtaining an extensive family history and a saliva sample - we don't expect the participants to be at risk. However, the only possible risk that may occur is in a situation where the privacy is at risk. We will try to minimize this by the arrangement as mentioned in this form.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Cases :
-are defined as consanguineous parents of a child that is affected by an autosomal recessive disorder
-This autosomal recessive disorder has not occurred in the family before.
Controls :
-are defined as consanguineous parents without (previous) affected children and with at least three healthy children.

In our study we restrict ourselves to couples with an inbreeding coefficient (F) of at least F= 1/128. This inbreeding coefficient must be clear from the family tree that include ALL third-degree family members (including great grandparents) of the couple, to make sure equally reliable and sufficient information is obtained in all pedigrees. ;Cohort:
Consanguineous couples with a desire to have children. There are no previous cases of autosomal recessive disorders in the family.

Exclusion criteria

- the nature of the disorder of the affected child is not clear
- the disease has occurred in the family before
- the inbreeding coefficient is less than 1/128

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-05-2009
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	28-10-2008
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	NL24748.029.08