Cardio-Genetic Basis of Sudden Infant Death Syndrome occurring in Temporal Association with Vaccination

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The objective of this study is to determine the frequency of previously undiagnosed SCN5A mutations leading to sudden death in temporal association with vaccination in The Netherlands.

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

Summary

ID

NL-OMON37517

Source
ToetsingOnline

Brief title
GENESIS

Condition

- Cardiac arrhythmias
- Cardiac and vascular disorders congenital

Synonym
"cot death" and "cardiac sodium channelopathies"

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cardiology, Genetics, SIDS, Vaccination

Outcome measures

Primary outcome

The study parameter is the identification of SCN5A mutations by genetic testing.

The endpoint of the study will be the completion of genetic testing in all

study subjects.

Genetic analysis of blood samples to detect SCN5A mutations will be performed

as per the protocol of the Department of Clinical Genetics, AMC.

Secondary outcome

Not applicable

Study description

Background summary

Sudden and unexpected death of an infant that remains unexplained after a thorough investigation of the circumstances, family history, a pediatric examination and a full autopsy is termed sudden infant death syndrome (SIDS). The etiology of SIDS is thought to be multifactorial and it is a diagnosis of exclusion. Cardiac sodium channel (SCN5A) mutations or channelopathies have been unravelled as an important cause of SIDS, underlying at least 10-15% of SIDS cases. Brugada Syndrome and Congenital Long QT Syndrome type 3, the classical disease manifestations of SCN5A mutations, can both be lethal conditions. The alteration of the delicate balance between inward and outward ionic currents across the cardiac cell membrane caused by these mutations are responsible for the potentially fatal ventricular arrhythmias in affected patients, especially during fever. Though uncommon in the pediatric population, affected children may present with life-threatening events.

Infant immunization is one of the most remarkable achievements of modern day medicine in terms of eradicating or drastically reducing mortality and morbidity due to serious childhood infections. However, there have been several reports of deaths following vaccination in apparently healthy infants, which

were diagnosed as SIDS. Our recent experience of sudden cardiac death in a 3 month old male and the occurrence of ventricular arrhythmias in a 4 month old female, both within 48 hours of receiving vaccination, and the subsequent diagnosis of SCN5A mutations in the patients and their siblings has triggered the idea for this study. We believe that there could be more to sudden deaths following vaccination than just SIDS, especially in vulnerable infants with undiagnosed sodium (SCN5A) channel mutations, particularly because fever has already been established as an arrhythmia-trigger in affected infants and it also happens to be the commonest side-effect of vaccination. The key to unravelling this association is by performing genetic testing of SIDS cases to look specifically for SCN5A mutations in cases where death was temporally associated with vaccination. In genetically confirmed subjects, family-screening will be carried out with clinical evaluation of all members followed by genetic counselling and predictive testing (if warranted) to identify the affected individuals. Adequate prophylactic measures such as aggressive antipyretics and hospitalisation and monitoring during vaccinations and fever episodes will be undertaken to prevent further mortality among siblings of the sudden death victim. As we strongly believe in the benefits of immunization to the individual and the community, we are convinced that this study will not only clarify some myths about vaccine-related deaths in infants thought to be *healthy* but will also pave the way for parental education and counselling regarding the underlying genetic condition and the prevention of sudden death due to vaccination and fever related ventricular arrhythmias

Study objective

The objective of this study is to determine the frequency of previously undiagnosed SCN5A mutations leading to sudden death in temporal association with vaccination in The Netherlands.

Study design

The study is designed as a cohort study. Study subjects will be drawn from the SIDS registry maintained by the Landelijke Werkgroep Wiegendood (LWW) in The Netherlands. Previously documented data on gender, age at death, occurrence of acute life-threatening events prior to death and any history of SIDS or sudden unexplained young deaths among family members will be retrieved. Genetic testing will be performed for SCN5A mutations using the stored neonatal heel-prick blood sample/stored DNA/stored tissue of each subject. In the event that stored material of a subject is unavailable or is unable to be used for genetic testing, both parents of the subject will be clinically evaluated and genetically tested for the presence of SCN5A mutations.

The study is estimated to take 3-6 months to complete. The LWW will provide the requisite data on the study subjects followed by which the genetic testing will be carried out at the Department of Clinical Genetics in AMC, Amsterdam.

Study burden and risks

The benefits of the study will be the identification of an underlying genetic cause for SIDS in the deceased victims or their parents which will enable subsequent family-screening and thereby prevention of sudden death of surviving relatives including the parents and siblings. Appropriate genetic counselling and follow-up care will be provided to the affected families at the Department of Clinical Genetics in the AMC with an aim to prevent potentially life-threatening arrhythmias. The benefits of the study far outweigh the risk of the possible implications on insurance that the results of the study might have. SIDS cases alone can serve as the study group due to the nature of the study analysing the frequency of SCN5A mutations in sudden death cases in temporal association with vaccination.

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

SIDS cases registered with the Landelijke Werkgroep Wiegendood (LWW) with death occurring within 14 days of BMR vaccination or within 3 days of any other vaccination

Exclusion criteria

None

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-11-2012
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO

Date:	23-08-2012
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	NL39175.018.12