Cardiac arrhythmias in Dravet syndrome

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We aim to to record heart rate patterns during seizures with miniaturized wearable EKG-monitors in a large cohort of DS

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

Summary

ID

NL-OMON41805

Source
ToetsingOnline

Brief title
Cardiac arrhythmias in Dravet syndrome

Condition

- Cardiac arrhythmias
- Seizures (incl subtypes)

Synonym
Dravet syndrome, epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Epilepsie Instellingen Nederland
Source(s) of monetary or material Support: Epilepsiefonds

Intervention

Keyword: Arrhythmias, Dravet syndrome, Sudden unexpected death in epilepsy

Outcome measures

Primary outcome

Ictal asystole (sinus arrest * 3 s) or ictal bradycardia (< 2nd heart rate

percentile for age)

Secondary outcome

Ictal QT lengthening or shortening

Study description

Background summary

Dravet syndrome (DS) is a severe childhood-onset epileptic encephalopathy with intractable seizures and developmental delay. Children with DS face a substantial risk of early epilepsy-related death: up to 15% by age 20.Sudden unexpected death in epilepsy (SUDEP) is the commonest cause of death in DS accounting for up to 60% of all mortality. SUDEP is the sudden unexpected death of a person with epilepsy in which a toxicological or anatomical autopsy is negative for a cause of death. SUDEP is most likely a seizure-related event and a high frequency of convulsions is the strongest risk factor. Currently, it is not preventable. The pathophysiology of SUDEP is poorly understood, but likely heterogeneous and multifactorial. The few available ictal recordings of SUDEP indicate that most deaths occur in the aftermath of a convulsion. Mechanisms including central cardiorespiratory dysfunction have been suggested. The relative low incidence of SUDEP, limited availability of ictal-recordings even in prospective multi-center registries14 and pathophysiological heterogeneity are critical barriers to develop preventative measures.
We suggest that DS may constitute a homogeneous subgroup of SUDEP as (1) its incidence is substantially higher than in other forms of severe childhood epilepsy,8,9 (2) SUDEP in DS occurs in childhood: this contrast with SUDEP where a older peak incidence is noted,15 (3) DS has a genetic basis: in >70% of DS cases de novo mutations/deletions in the SCN1A gene encoding for the *-subunit of the neuronal voltage-gated sodium channel Nav1.1 are found,6,7 (4) Nav1.1 channels are expressed in mammalian brain and heart.16 A SCN1A mutation may therefore confer a propensity for epilepsy and an innate vulnerability for cardiac arrhythmias, thus leading to a higher risk of SUDEP in DS.

Study objective

We aim to to record heart rate patterns during seizures with miniaturized wearable EKG-monitors in a large cohort of DS

Study design

International observational study with historical controls

Study burden and risks

Participation does not carry risks. The sensor is miniaturised and wearable, thus minimising discomfort. If this nevertheless may occur, the study can be immediately terminated. This study provides specific tools to investigate the seizure-related heart rate response. Subjects may thus benefit from participation by identification of otherwise unknown arrhythmias. The rationale of the study (the high SUDEP risk and the evidence in animal studies for arrhythmic cause of sudden death), specifically applies to DS, a rare epileptic syndrome including minors and incapacitated persons. We believe that the lack of risks, the potential diagnostic benefit, the minimal intervention with novel and wearable sensors and the possibility to terminate the study in case of discomfort, justifies the study in this patient group.

Contacts

Public
Stichting Epilepsie Instellingen Nederland

Achterweg 5
Heemstede 2103SW
NL
Scientific
Stichting Epilepsie Instellingen Nederland

Achterweg 5
Heemstede 2103SW
NL

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

1) Dravet syndrome with a known pathogenic SCN1A mutation
2) seizure frequency * 1/week (all seizure types expect for absences or myoclonias)
3) no self-harm
4) age * 6 years

Exclusion criteria

None

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:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-06-2015
Enrollment:	40

Type:	Actual

Medical products/devices used

Generic name:	nECG textile and nECG minder
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	27-03-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL48765.058.15

Study results

Date completed:	01-09-2018
Results posted:	18-07-2019

Actual enrolment: 48

Summary results
Trial is onging in other countries

First publication
18-07-2019