Phenomics & Genomics of Clozapine Pharmacotherapy - Current Users

Published: 23-09-2015
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Primary: To assess whether the genetic architecture of this severe SCZ phenotype differs from the broad DSM-based SCZ phenotype.To predict response and side effects after clozapine intakeSecondary:1. To detect genetic associations with the current...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Schizophrenia and other psychotic disorders
Study type	Observational non invasive

Summary

ID

NL-OMON50518

Source
ToetsingOnline

Brief title
CLOZIN Current Users

Condition

- Schizophrenia and other psychotic disorders

Synonym
psychosis, psychotic disorders

Research involving
Human

Sponsors and support

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

Intervention

Keyword: adverse reactions, clozapine, efficacy, genetics

Outcome measures

Primary outcome

To assess whether the genetic architecture of this severe SCZ phenotype differs

from the broad DSM-based SCZ phenotype.

Secondary outcome

To detect genetic associations with the current severe SCZ phenotype in healthy

participants (case-control comparison)

Study description

Background summary

Clozapine (CLZ) is generally prescribed if at least two trials of antipsychotic agents have not led to satisfactory clinical improvement, thereby implying that patients on clozapine generally suffer from more severe and/or persistent symptoms than SCZ patients on other antipsychotic agents. Unraveling the (functional) genetic variation underlying this severe SCZ phenotype therefore has the potential to deepen our understanding of the biological underpinnings of SCZ beyond the boundaries of DSM-based consensus criteria. Such knowledge in turn has the potential to shape future pharmacotherapeutic research. We here hypothesize that targeting this phenotype in genome-wide association studies and next-generation sequencing studies will signal genetic risk loci implicated in this severe SCZ phenotype. This is clinically relevant, because if we can identify whether SCZ patients are more severe patients immediately, we can start giving them clozapine as the first antipsychotic treatment. This might result in better outcomes, since every relapse a SCZ experiences, worsens the symptoms of this patient.

Study objective

Primary:
To assess whether the genetic architecture of this severe SCZ phenotype differs from the broad DSM-based SCZ phenotype.
To predict response and side effects after clozapine intake

Secondary:
1. To detect genetic associations with the current severe SCZ phenotype by performing a case-control comparison with healthy participants
2. To investigate whether CLZ use increases or decreases the risk of cardiovascular disease and early death.

Study design

This is a partly cross-sectional study in which both phenotypic and genotypic data are gathered from this study population that uses clozapine. A genome-wide association study (GWAS) will be performed to reveal possible differences in genetic architecture between patients on clozapine and the broad schizophrenia phenotype on the one hand and between those on clozapine and healthy controls on the other. Targeted next-generation sequencing may be used to follow-up possible positive associations.

Study burden and risks

Almost all patients on clozapine regularly have their blood drawn for routine white blood cell counts and/or clozapine blood level assessments. We anticipate that the majority of the study population will consist of such patients as white blood cell monitoring is strictly enforced in clinical practice for this patient group. For these patients, no risks will be attached to the study as the blood necessary for DNA extraction for the current study will be drawn from these routinely performed venipunctures. In addition, time investment for these participants will be negligible as there is only a 5 minute interview with their treating physician. A minority of patients on clozapine doesn*t have their blood routinely monitored. These subjects will be asked to allow a single blood draw, as well as the stopped users. A venipuncture entails the risk of a hematoma (blood leaving the vessel). We aim to minimize this risk by only allowing experienced personnel to draw blood and in the event of deeply located or thin veins request central lab personnel to perform the venipuncture. Although a hematoma resulting from a traumatic puncture imposes an esthetical burden on the subject, no serious health risks are involved. Should the venipuncture be traumatic or in the event of syncope and insufficient blood is obtained, we will give the participant the option to terminate his/her participation.

Contacts

Public
Universitair Medisch Centrum Utrecht

Universiteitsweg 100

Utrecht 3584 CG
NL
Scientific
Universitair Medisch Centrum Utrecht

Universiteitsweg 100
Utrecht 3584 CG
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-he/she currently uses clozapine or has used clozapine
-he/she has received a diagnosis of schizophrenia, schizophreniform, schizoaffective disorder or psychotic disorder NOS (DSM IV)/(un)specified schizspectrum or other psychotic disorder (DSM 5).
-his/her age must be >=18 years old
-he/she must be able to speak and read the Dutch language
-he/she must understand the information provided about the study and understand the consequences of participating and express a willingness to participate. This estimation is done by the treating physician during the informed consent procedure.

Exclusion criteria

- Involuntarily admission (unless allowed by local law)
- when the treating physician doubts if the patient understands the information/consequences of participation or the willingness to participate
- Patients with Parkinson*s disease

Study design

Design

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

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-01-2016
Enrollment:	2778
Type:	Actual

Ethics review

Approved WMO Date:	23-09-2015
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	28-06-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-12-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-07-2017
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	17-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-07-2020
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 20386
Source: NTR
Title:

In other registers

Register	ID
Other	5248
CCMO	NL52726.041.15
OMON	NL-OMON20386