Ketamine Trial Amsterdam (KETA), pilot

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26105

Source
Nationaal Trial Register

Brief title
KETA pilot

Health condition

(acute) suicidality, depression, personality disorders, substance use disorder.
(acute) suïcidaliteit, depressie, persoonlijkheidsstoornissen, middelenmisbruik

Sponsors and support

Primary sponsor: University Medical Center Amsterdam, location AMC
Source(s) of monetary or material Support: ZonMw, suicide prevention grant

Intervention

Outcome measures

Primary outcome

Change in suicidality scores on the Beck Scale for Suicidal Ideation (BSSI) between baseline and 180 minutes after 75 mg intranasal ketamine administration compared to 3.8 mg intranasal midazolam (placebo).

Secondary outcome

1. Suicidality from baseline to 60 minutes, 180 minutes, 1, 3 and 7 days and 6 and 12 months after one intranasal ketamine administration as measured with:

a. Beck Scale for Suicide Ideation (BSSI)

b. Suicidality item on the Montgomery Asberg Depression Rating Scale. (MADRS).

2. Actual number of suicides and suicidal acts in at 60 and 180 minutes, 1, 3 and 7 days and 6 and 12 months after ketamine/midazolam administration.

3. Depressive symptoms as measured with the MADRS from baseline to 60 and 180 minutes, 1, 3 and 7 days and 6 and 12 months after one intranasal ketamine administration compared to placebo.

4. Psychotomimetic symptoms, as measured with the Brief Psychiatric Rating Scale – Positive Subscale (BPRS) from baseline to 60 and 180 minutes.

5. Change in BDNF concentration, genetics and other biomarkers, and the correlation pattern between change in BDNF concentration and suicidality. Three blood samples will be taken by venepuncture at baseline: two samples into a vacuum tube containing ethylene diamine tetra-acetic acid (EDTA) that will be transferred into a heparinised tube, and one directly into a serum gel tube. At 180 minutes also three blood samples will be taken to measure the BDNF concentration. Two in an EDTA tube and one into a serum gel tube. Furthermore, at baseline one 9ml EDTA sample will be taken in order to study genetics.

6. Plasma ketamine concentration at 180 minutes.

7. Structural MRI, functional MRI (fMRI), diffusion tensor imaging (DTI), H-MRS-analysis of glutamate in hippocampus and prefrontal cortex. Subjects that were administered ketamine will be compared to subjects that were administered midazolam, at one day after administration.

8. A responder/non responder analysis. (Response is defined as a 50% reduction in BSSI-score) for the total study period.

9. Correlation patterns for the total study period between changes in BSSI- and MADRS-scores

10. Correlation patterns for the total study period between sex and changes in BSSI scores

Study description

Background summary

Rationale:

Suicide is currently one of the three leading causes of death in the Netherlands in people aged 15-44 and has a substantial impact on families and society. Nevertheless, to date no evidence based pharmacological intervention for acute suicidality exists. Subanesthetic doses of intravenous ketamine have been shown to immediately resolve depressive symptoms and suicidal ideation in depressed patients. However, this effect was never investigated for suicidality per se. Herewith, we propose a multicenter double blind randomized placebo controlled trial in 12 subjects as a pilot for the main study with 144 subjects, presenting with acute suicidality regardless of the underlying diagnosis, to test the hypothesis that a single dose of 75mg intranasal ketamine is able to diminish acute suicidal ideation and behaviour. Additionally, we will examine ketamine's anti-suicidal mechanism of action by measuring plasma, serum and neuroimaging markers. This study may result into a readily available and easily applicable intervention for the treatment of acute suicidality.

Objective:

To test the hypothesis that a dose of 75mg of intranasal ketamine lowers suicidal ideation and behaviour significantly more than active placebo: midazolam.

Study design and population:

This is a multicenter double blind randomized placebo controlled study: a total of 144 subjects will be included. They will receive an intranasal dose of 75mg ketamine or 3.8mg midazolam. At baseline and at 60 and 180 minutes, 1, 3 and 7 days and 6 and 12 months after ketamine administration, the Beck Scale for Suicide Ideation will be administered. Blood will be taken at 0 and 180 minutes to assess fatty-acid profiles, Brain Derived Neurotrophic Factor (BDNF) and ketamine concentrations. One day after administration, in persons who provided informed consent for participation in the imaging study, magnetic resonance scans will be performed (diffusion tensor imaging (DTI), resting state functional magnetic resonance imaging (fMRI) and magnetic resonance spectroscopy (MRS)).

Main study parameters/endpoints:

Primary: Change in suicidality scores on the Beck Scale for Suicidal Ideation (BSSI) between baseline and 180 minutes after 75 mg intranasal ketamine administration compared to 3.8 mg intranasal midazolam (placebo).
Secondary: Change in Montgomery Asberg Depression Rating Scale (MADRS), Brief Psychiatric Rating Scale – Positive Symptoms Subscale (BPRS-PS) (4), change in serum and plasma BDNF concentrations from 0 to 180 minutes, fatty acid concentrations at baseline, plasma ketamine concentrations at 180 minutes after intervention, functional and structural frontolimbic connectivity patterns, hippocampal volume and glutamate levels.

Nature and extent of the burden and risks associated with participation is considered negligible: The expected side effects of 75mg intranasal ketamine are minor. The most commonly described side-effect is a feeling of dissociation. To date, no serious adverse event related to the intervention has occurred in low-dose ketamine trials for mood disorders. The

expected benefit may be a significant in terms of immediate reduction of suicidal ideation and behaviour.

Study objective

A single subanesthetic dose of intranasal ketamine is able to diminisch acute suicidal ideation and behaviour, regardless of the underlying diagnosis.

Study design

T0 (baseline)

1 hour after intervention

3 hours

1 day

3 days

7 days

6 months

12 months

Intervention

-ketamine nasal spray 75 mg

-midazolam nasal spray 3,8 mg (active placebo)

Contacts

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Eligibility criteria

Inclusion criteria

-Acute suicidality: suicidal thoughts and/or behaviour have increased within the last 24 hours.

-score on the Beck Scale for Suicide Ideation (BSSI) > or = 7

Exclusion criteria

-Earlier participation in this study

-Psychosis

-Schizophrenia or another psychotic disorder

-History of PCP- or ketamine addiction

-Being under the influence of GHB (Substance abuse in the (recent) history is not an exclusion crtierion per se (with the exception of GHB and high blood alcohol concentration, and intoxications leading to medical unstable conditions)
Clinically significant and unstable infectious, immunological, neurological cardiovascular, gastro-intestinal, pulmonary, renal, ophthalmological (glaucoma), hepatic, endocrine or haematological disorder, a myocardial infarction, micturition problems or a complex surgical problem that needs immediate attention

-A known hypersensitivity for ketamine

-Concomitant use of a MAO-inhibitor

-Severe nose congestion or nasal polyps

-Pregnancy or giving breastfeeding

-Women using unreliable contraception

-Being unable to answer the questionnaires

-Legal incompetency

-No informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	20-08-2018
Enrollment:	12
Type:	Anticipated

Ethics review

Positive opinion

Date:	01-08-2018
Application type:	First submission

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
NTR-new	NL7215
NTR-old	NTR7414
Other	537001004 (ZonMw project number) : ABR 55438

Study results