Ketamine Trial for Acute suicidality - pilot

Published: 02-09-2020
Last updated: 13-01-2025

A dose of 75mg of intranasal ketamine lowers suicidal ideation

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20015

Source
NTR

Brief title
KETA-pilot

Health condition

Acute Suicidality

Sponsors and support

Primary sponsor: University Medical Center Groningen (UMCG)
Source(s) of monetary or material Support: ZonMw, Suicide Prevention Call

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.

Secondary outcome

1. Suicidality from baseline to 60 minutes, 180 minutes, 1, 3 and 7 days after one intranasal ketamine administration as measured with: a. Beck Scale for Suicide Ideation (BSSI) (Dutch version) b. Suicidality item on the Montgomery Asberg Depression Rating Scale. (MADRS) (Dutch version). 2. Actual number of suicides and suicidal acts at 60 and 180 minutes, 1, 3 and 7 days and after ketamine administration. 3. Depressive symptoms as measured with the MADRS from baseline to 60 and 180 minutes, 1, 3 and 7 days and after one intranasal ketamine administration compared to placebo. 4. Clinical severity and improvement as measured with the CGI. 5. Psychotomimetic symptoms, as measured with the SAFTEE (Dutch version) and the CADSS (Dutch version) from baseline to 60 and 180 minutes. 6. 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 (61). Furthermore, at baseline one 9ml EDTA sample will be taken in order to study genetics. (See table 1) 7. Plasma ketamine concentration at 180 minutes. 8. Structural MRI, functional MRI (fMRI), diffusion tensor imaging (DTI), H-MRS-analysis of glutamate in hippocampus and prefrontal cortex, at one day after ketamine administration. 9. A responder/non responder analysis. (Response is defined as a 50% reduction in BSSI-score) for the total study period. 10. Correlation patterns for the total study period between changes in BSSI- and MADRS-scores. 11. 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 (1). 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 (2, 3). However, this effect was never investigated for suicidality per se. Herewith, we propose a multicenter double blind randomized placebo controlled trial in 100 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: The objective of the main KETA-study is to test the hypothesis that a dose of 75mg of intranasal ketamine lowers suicidal ideation and behaviour significantly more than active placebo: midazolam. First, a feasibility pilot with 12 subjects, who will all receive ketamine, will be performed. Study design and population: This is a feasibility pilot study for the larger KETA-trial: a total of 12 subjects will be included. They will receive an intranasal dose of 75mg . At baseline and at 60 and 180

minutes, 1, 3 and 7 days 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)). Prior to the RCT, we will perform a small-scale feasibility study in the UMCG (n=12), which is described in paragraph 8.3.1. 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. Secondary: Change in Montgomery Asberg Depression Rating Scale (MADRS), the Clinical Global Impression (CGI), the Systematic Assessment for Treatment Emergent Events (SAFTEE) and the Clinician Administered Dissociative States Scale (CADSS) (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 moderate: 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. However, all participants that are to be included, have a high risk of attempting or committing suicide, therefore, the chance that a SAE might occur, is relatively high, and we will therefore classify the risk level of this study as moderate. The expected benefit may be significant in terms of immediate reduction of suicidal ideation and behaviour.

Study objective

A dose of 75mg of intranasal ketamine lowers suicidal ideation

Study design

T0, T 1 hour, T3 hours, T1 day, T3 days, T7 days.

Intervention

intranasal ketamine

Contacts

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Eligibility criteria

Inclusion criteria

Acute suicidality: suicidal thoughts and/or behaviour have increased within the last 24 hours. BSSI score ≥ 7 Subjects are in the age of 18-70

Exclusion criteria

Earlier participation in this study Psychosis (as a primary diagnosis) (depression with psychotic features will not be an exclusion criterion per se). Schizophrenia or another primary psychotic disorder History of PCP- or ketamine addiction Being under influence of GHB (Substance abuse in the (recent) history is not an exclusion criterion per se (with the exception of current GHB-intoxication and a high blood alcohol concentration, and intoxications leading to medical unstable conditions). Use of GHB will be assessed by asking the participant, since urinary analysis is relatively unreliable, and waiting for results of the blood test will, given the acute nature of this study, be too time consuming. A blood alcohol concentration (BAC) of > 0.05% 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. Presence of any contra-indication for ketamine use, such as severe high blood pressure, a recent myocardial infarction or relevant cardiac problems, severe thyroid problems, severe liver problems, severe kidney problems, epilepsy and increased intracranial pressure. A known hypersensitivity for ketamine Concomitant use of a MAO-inhibitor Severe nose congestion or nasal polyps Pregnancy or giving breastfeeding Women in the reproductive age using unreliable contraception Being unable to answer the questionnaires Legal incompetency with regard to participation in this study No informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	02-09-2020
Enrollment:	12
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 52646
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8873
CCMO	NL74304.042.20
NTR-new	NL3213
NTR-old	NTR3364
Other	EudraCT : 2011-001820-39
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON52646

Study results