Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

The effect of Hydralazine on early stage of Alzheimer’s disease: A randomized clinical trial

Protocol summary

Study aim

1) Determination and comparison of the effect of 75mg (25mg TDS) Hydralazine vs. placebo in patients with mild to moderate Alzheimer’s disease 2) Development of an electronic Case Report Form and push notification system to remind patients (and caregivers) to take the medications to improve drug adherence and reduce losses to follow-up. 3) Evaluation of the prognostic ability of olfactory tests to predict the changes in cognition and performance of patients with mild to moderate Alzheimer's disease.

Design

This is a phase III, triple-blind, parallel double armed randomized clinical trials with allocation ratio of 1-1 to the intervention and placebo arms. This trial will be conducted on 424 randomly selected patients using random permuted blocks.

Settings and conduct

All patients who are identified as potentially eligible by the supporting neurologists and psychiatrists will be referred to Yazd Rahnemoon Hospital (YRH) to evaluate their cognitive function. The two arms of the study are Hydralazine 75mg (25mg three times per day) or Hydralazine placebo. Follow-up evaluation will continue for one year after drug administration. The participant, outcome assessors, researchers and data analyzer will be blinded to the study arms.

Participants/Inclusion and exclusion criteria

patients over the age of 50 who are diagnosed with mild to moderate AD are included in the study; dementia patients with etiologies other than AD (i.e. vascular related) are not included.

Intervention groups

The two arms of the study are Hydralazine 75mg (25mg three times per day) or Hydralazine placebo.

Main outcome variables

Various cognitive and function tests for patient and caregiver, olfactory tests, biochemistry as well as drug side effects will be assessed regularly over the period of follow up.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20200711048075N1**
Registration date: **2020-07-29, 1399/05/08**
Registration timing: **prospective**

Last update: **2020-07-29, 1399/05/08**
Update count: **0**

Registration date

2020-07-29, 1399/05/08

Registrant information

Name

Masoud Mirzaei

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-09-22, 1399/07/01

Expected recruitment end date

2023-09-23, 1402/07/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title
The effect of Hydralazine on early stage of Alzheimer’s disease: A randomized clinical trial

Public title
Effect of Hydralazine on Alzheimer’s disease

Purpose
Prevention

Inclusion/Exclusion criteria

Inclusion criteria:
Diagnoses of possible or probable Alzheimer's disease (NINCDS-ADRDA). Presence of a caregiver (friend or relative) who can assume responsibility for medication administrations, accompany the patient to all visits, and rate patient's condition. Written informed consent from both the patient (or surrogate) and caregiver. An MMSE score between 12 and 26 inclusive. Administration of a maintenance dosage of donepezil (5-10mg/d), rivastigmine (3-6mg/d), galantamine or galantamine ER (8-16mg/d) for a minimum of 4 weeks prior to randomization. Agreement not to take Hydralazine. Age 49 and over

Exclusion criteria:
A non-Alzheimer primary dementia (e.g., vascular dementia, Lewy body dementia, frontotemporal dementia, vitamin B-12 deficiency, hypothyroidism). Current major depression, delirium, alcohol or psychoactive substance abuse or dependency, schizophrenia, or delusional disorder as defined by DSM-IV. Presence of any uncontrolled systemic illness that would interfere with participation in the study or a life expectancy of less than one year. Currently being treated with Hydralazine or a history of intolerance to oral therapy with Hydralazine Any intravenous treatment for heart failure, except IV furosemide (e.g. IV inotropes, pressors, nitrates or nesiritide) at the time of screening. Systolic blood pressure <100 mmHg Reversible etiology of acute heart failure such as myocarditis, acute myocardial infarction-over the past 4 weeks, arrhythmia and pacing device (Acute MI is defined as symptoms and major electrocardiogram (ECG) changes(i.e., ST segment elevations), and arrhythmia includes unstable heart rates above 120/min or below 50/min). Known severe congenital heart disease (such as uncorrected tetralogy of fallot or transposition of the aorta) and severe aortic or mitral stenosis or severe rheumatic mitral regurgitation. Concurrent use of phosphodiesterase type 5 (PDE5) inhibitors (e.g. Viagra, Sildenafil. Etc.) Have had cardiac revascularisation within the last 3 months or are likely to require coronary revascularisation within the study period. eGFR< 15ml/min/1.73m2, or on regular dialysis, or planned dialysis within the study period

Age
From **49 years** old

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: **424**

Randomization (investigator's opinion)
Randomized

Randomization description
The treatment allocation ratio for the two treatment arms will be 1:1. The random sequence will be extracted and the randomization process will be permuted block randomization. Each block consists of four participants. Treatment scheme which will be generated by sealed envelope (https://www.sealedenvelope.com/) website. The prepackaged study medications complied by Iran FDA, will be delivered at the pharmacy of YRH to each participating patient. The medications will be provided in identical boxes. Each box will bear a unique medication identification number.

Blinding (investigator's opinion)
Triple blinded

Blinding description
The participant, outcome assessors, researchers and data analyzer will be blinded to the study arms.The site personnel will be blinded to the medication and treatment assignment. The EHSAN website will assign the blinded medication box numbers for the patient. The box number will be assigned based on the random treatment scheme generated by the website. For each subsequent refill of study medication, the site will log on to the EHSAN website to obtain a new medication box number, which will also be linked to the randomization scheme. The patient will begin treatment the same day as randomization. The study blind will not be broken at the time a patient is withdrawn from the trial. The blind will be broken at the conclusion of the trial for all randomized patients.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
National Institute for Medical Research

Street address
No. 21, Besat St. W. Fatemi Ave. Tehran-Iran

City
Tehran

Province
Tehran

Postal code
1419693111

Approval date
2019-06-16, 1398/03/26
Ethics committee reference number
IR.NIMAD.REC.1398.424

Health conditions studied

1

Description of health condition studied
Alzheimer’s disease
ICD-10 code
G30.0
ICD-10 code description
Alzheimer's disease with early onset

Primary outcomes

1

Description
The progression of of Alzheimer's disease
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
ADAS-cog inventory

Secondary outcomes

1

Description
Function of Alzheimer's patients
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
Lawton Activity of Daily Living Scale

2

Description
Cognition of Alzheimer's patients
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
Mini Mental State Examination

3

Description
Behavior of Alzheimer's patients
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
Nero-Psychiatry Inventory

4

Description
Caregiver time
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
Caregiver Activity Scale

5

Description
Olfactory sense
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
Olfactory test

6

Description
Drug side effects
Timepoint
Before the intervention - 3/6/9/12 months after the start of the intervention
Method of measurement
Blood biochemistry tests

Intervention groups

1

Description
Intervention group: Hydralazine 75mg (25mg three times per day)
Category
Treatment - Drugs

2

Description
Placebo 25 mg TDS
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Adineh Health Centre
Full name of responsible person
Behnam Bagheri
Street address
No. 16, Shohada St, Daneshjoo Blvd. Yazd
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Postal code

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
National Institute for Medical Research Development

Full name of responsible person
Professor Reza Malekzadeh

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http://rms.nimad.ac.ir

Grant name
Neuro-psychiatry Division (Main Grant)

Grant code / Reference number
964744

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
National Institute for Medical Research Development

Proportion provided by this source
89

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

2

Sponsor

Name of organization / entity
Kereshmeh Food Co.

Full name of responsible person
Ali Maleki

Street address
No,1- 61th Street, Azadegan Blvd. Yazd-Iran

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Phone
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Email
info@kereshme.com

Grant name
Social responsibility

Grant code / Reference number
1898- 29.06.1396

Is the source of funding the same sponsor organization/entity?
No

Title of funding source
Kereshme Food Co.

Proportion provided by this source
11

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Yazd University of Medical Sciences

Full name of responsible person
Nastaran Ahmadi

Position
Assistant Professor (Research)

Latest degree
Ph.D.

Other areas of specialty/work
Epidemiology

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Yazd Cardiovascular Research Centre, Afshar Heart Centre, Jomhouri Blvd, Yad-Iran

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ahmadi.psy@gmail.com

Web page address

https://web.ssu.ac.ir/index.aspx?tempname=ghalbyazd&lang=1&sub=70

Person responsible for scientific inquiries

Contact

Name of organization / entity
Yazd University of Medical Sciences

Full name of responsible person
Masoud Mirzaei

Position
Professor

Latest degree
Medical doctor

Other areas of specialty/work
Preventive Medicine

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Person responsible for updating data

Contact

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Yazd University of Medical Sciences

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Assistant Professor (Research)

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Other areas of specialty/work
Psychology

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Web page address
https://web.ssu.ac.ir/index.aspx?tempname=ghalbyazd&lang=1&sub=70

Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available

Study Protocol
Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form
Yes - There is a plan to make this available

Clinical Study Report
Yes - There is a plan to make this available

Analytic Code
Yes - There is a plan to make this available

Data Dictionary
Yes - There is a plan to make this available

Title and more details about the data/document
Study protocol, code books and data files

When the data will become available and for how long
After study site close down by the study monitor

To whom data/document is available
only available for people working in academic institutions.

Under which criteria data/document could be used
Chief Investigator: mmirzaei@ssu.ac.ir User and password will be provided for external monitors to have access to the study Case Report Form (CRF)

From where data/document is obtainable
Chief Investigator: mmirzaei@ssu.ac.ir User and password will be provided for external monitors to have access to the study Case Report Form (CRF)

What processes are involved for a request to access data/document
Contacting the Chief Investigator: mmirzaei@ssu.ac.ir

Comments