

Clinical Trial Protocol

Iranian Registry of Clinical Trials

12 Jul 2026

Evaluation and comparison of efficacy of atropine eye drops and ipratropium bromide oral spray and amitriptyline tablet in the management of clozapine-induced sialorrhea in patients with refractory schizophrenia using the TNHS(Toronto Nocturnal in the management of clozapine-induced sialorrhea in patients with refractory schizophrenia using the TNHS(Toronto Nocturnal Hypersalivation) scale Hypersalivation) scale

Protocol summary

Study aim

Evaluation and comparison of efficacy of atropine eye drops and ipratropium bromide oral spray and amitriptyline tablet in the management of clozapine-induced sialorrhea

Design

Clinical trial without control group and in parallel and one-way blind and randomized by the following method and in phase 2 for six months cross-sectionally on schizophrenic patients with DSM-V criterion diagnosis. For random allocation, the quadruple random permutation block method is used. A represents the person receiving the atropine drop and B represents the person receiving the spray Is ipratropium. The total number of 4 permutation block states is equal to 6 (BABA, ABAB, BAAB, ABBA, BBAA, AABB (; we assign 0 to 9 to each of the states (using a random number table).

Settings and conduct

In this cross-sectional study, patients with schizophrenia were randomly assigned to Imam Reza Clinic, Ibn Sina Hospital, and Hafez Hospital. For one month, each patient should be evaluated according to the TNHS scale for the management of clozapine-induced sialorrhea. It should be noted that the study is a single-blind study. In this way, the medicines are given to the doctor in numbered envelopes, then he gives the medicine to the patient without knowing the contents of the envelopes.

Participants/Inclusion and exclusion criteria

Patients between the ages of 18 and 65 with a diagnosis of schizophrenia without comorbid conditions such as Parkinson's or cerebral palsy that cause sialorrhea, as

well as no pregnancy and lactating.

Intervention groups

In this study, patients with schizophrenia were randomly assigned to take one of the drugs amitriptyline, atropine drops, and ipratropium bromide nasal spray for one month according to the TNHS scale are supposed to be evaluated.

Main outcome variables

Reduction of clozapine-induced sialorrhea through intervention of atropine drops, ipratropium spray and amitriptyline tablets

General information

Reason for update

Acronym

CIH

IRCT registration information

IRCT registration number: **IRCT20211110053031N1**

Registration date: **2022-06-14, 1401/03/24**

Registration timing: **prospective**

Last update: **2022-06-14, 1401/03/24**

Update count: **0**

Registration date

2022-06-14, 1401/03/24

Registrant information

Name

Fatema Mohammadgholizad

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone +98 44 3344 3294	Phase 2
Email address pha.fa.chess@gmail.com	Groups that have been masked • Care provider
Recruitment status Recruitment complete	Sample size Target sample size: 1
Funding source	Randomization (investigator's opinion) Randomized
Expected recruitment start date 2022-07-24, 1401/05/02	Randomization description For random allocation, the quadruple random permutation block method is used. A represents the person receiving the atropine drop and B represents the person receiving the spray Is ipratropium. The total number of 4 permutation block states is 6 (BABA, ABAB, BAAB, ABBA, BBAA, AABB; you assign 0 to 9 to each of the states (using a random number table). And then we produce 12 blocks of 4 (12 * 4 = 48) until 48 people are randomly assigned to two groups.
Expected recruitment end date 2023-01-21, 1401/11/01	Blinding (investigator's opinion) Single blinded
Actual recruitment start date empty	Blinding description The study is a blind. In this way, only the treating physician does not know what kind of medicine he prescribes, and thus the medicines are placed in numbered envelopes and given to patients.
Actual recruitment end date empty	Placebo Not used
Trial completion date empty	Assignment Parallel
Scientific title Evaluation and comparison of efficacy of atropine eye drops and ipratropium bromide oral spray and amitriptyline tablet in the management of clozapine-induced sialorrhea in patients with refractory schizophrenia using the TNHS(Toronto Nocturnal in the management of clozapine-induced sialorrhea in patients with refractory schizophrenia using the TNHS(Toronto Nocturnal Hypersalivation) scale Hypersalivation) scale	Other design features
Public title Evaluation and comparison of efficacy of atropine eye drops and ipratropium bromide oral spray and amitriptyline tablet in the management of clozapine-induced sialorrhea	Secondary Ids empty
Purpose Treatment	Ethics committees <u>1</u>
Inclusion/Exclusion criteria Inclusion criteria: Patients aged 18 to 65 years with a diagnosis of schizophrenia according to the DSM-V criteria Patients should be receiving clozapine for at least 30 days Patients should have a minimum score of 2 on the TNHS scale for sialorrhea Exclusion criteria: Development of allergies or history of allergies to amitriptyline, atropine and ipratropium bromide Has an underlying disease such as Parkinson's or cerebral palsy that causes sialorrhea The patient has problems and comorbidities such as untreated constipation or urinary retention or bladder obstruction Concomitant use of drugs such as tricyclic antidepressants and atropine and ipratropium bromide and other anticholinergic drugs Breastfeeding and pregnancy History of diseases such as myasthenia gravis, seizures, cardiac arrhythmias, glaucoma, pyloric obstruction, prostate hypertrophy, renal failure, severe autonomic dysfunction, mental retardation, and paralytic paralysis	Ethics committee Name of ethics committee Ethics committee of Shiraz University of Medical Sciences Street address Vice-Chancellor for Research, Shiraz University of Medical Sciences, Zand Blvd., Shiraz, Iran City Shiraz Province Fars Postal code 711345-1978
Age From 18 years old to 65 years old	Approval date 2021-11-16, 1400/08/25
Gender Both	Ethics committee reference number IR.SUMS.REC.1400.619
	Health conditions studied

1

Description of health condition studied

Clozapine-resistant schizophrenic patients with clozapine-induced sialorrhea

ICD-10 code

F20

ICD-10 code description

Schizophrenia

Primary outcomes

1

Description

Effectiveness score of amitriptyline in reducing clozapine-induced sialorrhea according to TNHS (Toronto Nocturnal Hypersalivation scale)

Timepoint

At the beginning of the study, then daily for 7 days, then on days 14, 21 and 28

Method of measurement

Toronto Nocturnal Hypersalivation scale

2

Description

The effectiveness of atropine eye drops in reducing clozapine-induced sialorrhea according to the TNHS Toronto Nocturnal Hypersalivation Scale

Timepoint

At the beginning of the study, then daily for 7 days, then on days 14, 21 and 28

Method of measurement

Toronto Nocturnal Hypersalivation scale

3

Description

Effective score of ipratropium bromide nasal spray in reducing clozapine-induced sialorrhea according to TNHS (Toronto Nocturnal Hypersalivation scale)

Timepoint

At the beginning of the study, then daily for 7 days, then on days 14, 21 and 28

Method of measurement

TNHS (Toronto Nocturnal Hypersalivation scale)

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: In this group, patients are supposed to receive amitriptyline tablets from Iran Daroo Company at a dose of 25 mg first, and if the clozapine-induced sialorrhea complication does not improve with this dose of amitriptyline, then the dose of amitriptyline can be increased to 100 mg, Administered overnight before

bedtime.

Category

Treatment - Drugs

2

Description

Control group: In this group, patients are supposed to use 1% atropine eye drops sublingually from Sinadaru company as one drop three times a day, and if the patient has sialorrhea over night, he can take an extra drop Dissolved in a glass of water and gargle and spill it out. The maximum dose is two drops three times per day.

Category

Treatment - Drugs

3

Description

Intervention group: In this group, patients are supposed to use 0.03% ipratropium bromide nasal spray as one puff twice a day sublingually. If sialorrhea is not controlled, the maximum dose that can be used is two puffs twice a day.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Ebnesina hospital

Full name of responsible person

Fatemeh Mohammadgholizad

Street address

Shiraz, Hafez St., next to 13 Aban Park, Ibn Sina Medical Educational Center, Shiraz

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Postal code

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2

Recruitment center

Name of recruitment center

Imam Reza clinic

Full name of responsible person

Fatemeh Mohammadgholizad

Street address

Shiraz, Namazi Square, next to Namazi Hospital, Imam Reza (AS) Specialized and Sub-Specialized Clinic

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3

Recruitment center

Name of recruitment center
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Full name of responsible person
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Shiraz University of Medical Sciences
Proportion provided by this source
100

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

Person responsible for general inquiries

Contact

Name of organization / entity
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Full name of responsible person

Fatema Mohammadgholizad

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Latest degree

Specialist

Other areas of specialty/work

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Sharing plan**Deidentified Individual Participant Data Set (IPD)**

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

Study Protocol

No - There is not 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

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

Clinical Study Report

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

Analytic Code

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

Data Dictionary

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