Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

A comparative study of the effect of black mulberry and honey syrup with benzydamine hydrochloride mouthwash on the prevention of oral mucositis caused by radiation therapy in patients with head and neck cancer

Protocol summary

Study aim

General Objective: To compare the effect of black mulberry–honey syrup and benzydamine mouthwash on the prevention of radiotherapy-induced oral mucositis in head and neck cancer patients. Specific Objectives: -To assess and compare oral mucositis severity (weekly). -To assess and compare pain intensity (daily during radiotherapy). -To assess and compare quality of life (baseline, week 3, end of RT, and 2 weeks post-RT). -To assess and compare the time to onset of grade 1–2 oral mucositis.

Design

A randomized, controlled, parallel-group clinical trial (phase 2–3) on 80 patients. Randomization will be performed using Random Allocation Software version 2.

Settings and conduct

The study will be conducted at Imam Khomeini Hospital, Sari, Iran

Participants/Inclusion and exclusion criteria

Inclusion criteria: -Life expectancy more than 1 year -Karnofsky performance status more than 50 -Willingness to participate -At least two oral mucosal subsites in the radiotherapy field -No allergy to black mulberry or honey Exclusion criteria: -Prior radiotherapy/chemotherapy in oral or oropharyngeal region within 6 months -Active oral infection or ulcer before radiotherapy -Pregnancy

Intervention groups

Intervention group: Patients with head and neck cancer eligible for radiotherapy who meet the inclusion criteria and receive the black mulberry–honey syrup. Control group: Patients with head and neck cancer eligible for radiotherapy who meet the inclusion criteria and receive benzydamine hydrochloride mouthwash.

Main outcome variables

Primary outcome: Oral mucositis severity Secondary outcomes: Oral pain intensity (using the Visual Analogue Scale, VAS) Quality of life (using the EORTC QLQ-H&N35 questionnaire)

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20250928067392N1**
Registration date: **2025-10-10, 1404/07/18**
Registration timing: **prospective**

Last update: **2025-10-10, 1404/07/18**
Update count: **0**

Registration date

2025-10-10, 1404/07/18

Registrant information

Name

Ali Moghadami

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2025-10-23, 1404/08/01

Expected recruitment end date

2027-05-20, 1406/02/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A comparative study of the effect of black mulberry and honey syrup with benzydamine hydrochloride mouthwash on the prevention of oral mucositis caused by radiation therapy in patients with head and neck cancer

Public title

Comparison of black mulberry and honey syrup with benzydamine mouthwash in preventing mouth sores caused by radiotherapy in patients with head and neck cance

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

above 18years old Patients with head and neck cancer candidates for radiotherapy Life expectancy of more than one year as estimated by the physician or medical team Physical and mental ability to cooperate in completing the questionnaire with a Karnofsky performance status > 50 Willingness to participate in the study Presence of at least two subsites of the oral mucosa within the radiotherapy field No known allergy to black mulberry or honey

Exclusion criteria:

Previous radiotherapy and history of chemotherapy within the last six months in the oral cavity and oropharynx region Presence of active oral infection or ulcer before initiation of radiotherapy Pregnancy

Age

From **18 years** old

Gender

Both

Phase

2-3

Groups that have been masked

No information

Sample size

Target sample size: **80**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization will be performed by a biostatistician. Patients will be assigned into two groups, and the study medications will be distributed by the researcher. Recruitment will be carried out in parallel for both groups with an allocation ratio of 1:1. For randomization, a block randomization method will be used. Accordingly, patients will be numbered consecutively from 1 to 80 upon enrollment. The unit of randomization will be individual patients, and randomization will be performed using blocks of four. The type of group allocation for each patient will be determined using the Random Allocation Software version 2. To generate the random sequence, the software will produce codes “A” and “B,” where code A indicates allocation to the intervention group and code B indicates allocation to the control group. The generated codes will be placed in sealed, opaque envelopes, each labeled with the patient’s serial number. Upon the patient’s entry into the study, the physician will open the corresponding envelope and apply the assigned intervention. Completion of the demographic, clinical symptoms, and medical history forms will be performed by the principal investigator. The contact number of the investigator will be given to participants so that they can report any problems with the medication or their condition. In case a patient does not attend after the treatment period, follow-up will be conducted via telephone by the investigator.

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committees of Mazandaran University of Medical Sciences

Street address

Khazar Blvd, Faculty of Persian Medicine

City

Sari

Province

Mazandaran

Postal code

4846895475

Approval date

2025-09-23, 1404/07/01

Ethics committee reference number

IR.MAZUMS.REC.1404.297

Health conditions studied

1

Description of health condition studied

Radiotherapy-induced oral mucositis

ICD-10 code

ICD-10 code description

Primary outcomes

1

Description

Oral Mucositis Severity

Timepoint

Assessment of oral mucositis severity every week from the start of intervention until two weeks after its completion

Method of measurement

Examination by a radio-oncology specialist based on the World Health Organization (WHO) oral mucositis scale.

Secondary outcomes

1

Description

Oral pain

Timepoint

Daily until two weeks after the completion of the intervention.

Method of measurement

Visual Analogue Scale

2

Description

Quality of Life

Timepoint

Basis of intervention, third week of intervention, end of intervention, and two weeks after completion of intervention

Method of measurement

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Head & Neck 35

Intervention groups

1

Description

Intervention group: Patients with head and neck cancer who are candidates for radiotherapy and meet the inclusion criteria will receive the mulberry and honey preparation. The standardized mulberry extract and standardized honey (with necessary approvals such as microbial testing) will be obtained from a reputable company approved by the Food and Drug Administration and will be produced in the form of an oral syrup (manufactured by Giah Kala Company). The dosage will be 5 mL of mulberry-honey syrup per administration, which should be kept in the mouth for 15 seconds and then swallowed.

Category

Treatment - Drugs

2

Description

Control group: Patients with head and neck cancer who are candidates for radiotherapy and meet the inclusion criteria will receive benzydamine hydrochloride mouthwash. The prescribed regimen consists of three daily doses during radiotherapy, with 15 mL per dose, to be kept in the mouth for 30 seconds and then expelled.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Imam Khomeini hospital

Full name of responsible person

Seyde Sedighe Yousefi

Street address

Razi st, Sari

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emamsari.hospital@gmail.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Mazandaran University of Medical Sciences

Full name of responsible person

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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

Mazandaran 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
Mazandaran University of Medical Sciences
Full name of responsible person
Seyde Sedighe Yousefi
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Associate professor
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is 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
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
Title and more details about the data/document
Title of documents/data: De-identified patient data (primary and secondary outcomes) Details: Data on oral mucositis severity, pain (VAS), and quality of life (EORTC QLQ-H&N35) will be available for sharing in a de-identified form after removal of personal identifiers.
When the data will become available and for how long
De-identified data will be available to researchers starting 6 months after the publication of the results and will remain accessible for 5 years after publication
To whom data/document is available
De-identified data will be available to researchers affiliated with universities or recognized research institutions, upon request and after approval by the ethics committee.
Under which criteria data/document could be used
Data will be provided solely for research and scientific purposes in accordance with the objectives stated in the request; commercial use is not permitted. Analyses must align with the research plan submitted in the request; changing the primary objectives is not allowed. Data will

be de-identified, and the applicant is required to maintain confidentiality and must not attempt to re-identify participants. Use of the data is subject to approval by the ethics committee and the principal investigator. In any reports or publications, data must be presented anonymously, preserving participant identity. Upon completion of analyses, the applicant is required to provide the final results or research report to the principal investigator upon request

From where data/document is obtainable

Researchers wishing to access de-identified data must submit a formal request to the principal investigator. The request should include the intended use of the data, a proposed research plan, and a commitment to maintain data confidentiality. After review and approval by the ethics committee and the principal investigator, the data will be provided in secure, de-identified files. The review and data provision process typically takes 2 to 4 weeks.

What processes are involved for a request to access data/document

The applicant submits a formal request to the principal investigator, including the intended use of the data, a description of the proposed research plan, and a commitment to maintain data confidentiality. The principal investigator reviews the request and, if complete, forwards it to the ethics committee for approval. Upon approval by the ethics committee and the principal investigator, the de-identified data will be provided to the applicant in secure files. The entire process, from submission of the request to receiving the data, typically takes 2 to 4 weeks

Comments