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Comparison of different treatments in the management of recurrent herpes labialis

Submission date
25/08/2023

Recruitment status
No longer recruiting

Registration date
04/09/2023

Overall study status
Completed

Last Edited
21/01/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Recurrent herpes labialis results from reactivation of the latent herpes simplex type 1 virus. The injury is characterized by redness of the skin (erythema) and a small raised area of skin of papule that turns into vesicles filled with fluid rich in viral particles. Subsequently, these vesicles rupture, leading to ulceration and eventual crusting, initial symptoms precede these lesions in 46-60% of instances, and the healing process lasts between 10-8 days. This study aims to evaluate the effectiveness of low-level laser and olive leaf extract in the management of recurrent herpes labialis by comparing each treatment with acyclovir (the standard treatment).

Who can participate?
Patients aged over 18 years old who have a herpes labialis lesion in the vesicular stage

What does the study involve?
The patient sample will be randomly distributed among the groups according to the treatment method used:
Group 1 (the control group): (n = 20) application of topical acyclovir (Veramid 5%), 5 times/ 5 days, with the application of an inactive laser
Group 2: (n=20) application of diode laser (650 nm,100 mW) on the first day and after 48 hours, in addition to placebo cream
Group 3: (n=20) treatment with olive leaf extract in the form of a combined emollient and gel (emolgel), 5 times/ 5 days, with the application of an inactive laser.

What are the possible benefits and risks of participating?
The benefits of this study are the results that investigate safer alternatives to traditional antivirals for the management of recurrent herpes labialis. There are no possible risks of participating, only that it is possible that accelerated healing and rapid pain relief do not occur.

Where is the study run from?
Damascus University (Syria)

When is the study starting and how long is it expected to run for?
June 2021 to January 2024

Who is funding the study?
Damascus University – Funder No. 501100020595 (Syria)

Who is the main contact?
Mai Gaizeh Al-Hallak, memogh.1995mai@gmail.com

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2640

Study information

Scientific Title
A comparative study between low-level laser therapy (LLLT) and olive leaf extract (OLE) in the management of recurrent herpes labialis (RHL)

Study objectives
Current study hypothesis 21/01/2025:
For the pain variable:
1. Null hypothesis H0: There are no statistically significant differences in the effectiveness of the three treatments used in the studied groups.
2. Alternative Hypothesis H1: There are statistically significant differences in the effectiveness of the three treatments used in the studied groups.

For the healing speed variable:
1. Null hypothesis H0: No statistically significant differences exist in the effectiveness of the three treatments used in the studied groups.
2. Alternative Hypothesis H1: There are statistically significant differences in the effectiveness of the three treatments used in the studied groups.

Previous study hypothesis:
For the pain variable:
1. Null hypothesis H0: There are no statistically significant differences in the effectiveness of the four treatments used in the studied groups.
2. Alternative Hypothesis H1: There are statistically significant differences in the effectiveness of the four treatments used in the studied groups.

For the healing speed variable:
1. Null hypothesis H0: No statistically significant differences exist in the effectiveness of the four treatments used in the studied groups.
2. Alternative Hypothesis H1: There are statistically significant differences in the effectiveness of the four treatments used in the studied groups.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 02/08/2021, Scientific Research Council (Baramkeh, Damascus, 00963, Syria; +9693935423239; info@damascusuniversity.edu.sy), ref: 2640

Study design
Randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home, Laboratory, University/medical school/dental school

Study type(s)
Treatment, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Patients with recurrent herpes labialis

Interventions
Current interventions as of 14/01/2025:
This is a randomized controlled clinical study in which the patient sample will be divided into three equal groups according to the method of treatment used, and clinical evaluation will be conducted by blinded researchers who do not know of the type of treatment that will be used.

The sample will consist of 60 patients with recurrent herpes labialis in the vesicular stage over the age of 18 who are reviewers of the Department of Oral Medicine at Damascus University. The sample size was calculated using the G-power program.

Sample randomization:
The sample will be distributed among the three groups using an envelope containing 60 cards numbered from 1-3, where the patient takes the card corresponding to the number of the treatment group.

Methodology:
Firstly, written informed consent must first be obtained from the patient after being informed of the aims and methods of the current study. Secondly, patients will be screened to ensure they meet the inclusion criteria, then patients will be randomized into four study groups.

Interventional groups:
Group 1: Drug therapy with acyclovir: A preparation containing acyclovir at a concentration of 5% (Veramid from Medico) will be applied five times daily to the lesion site for 5 days. A placebo laser will also be applied to the site of the lesion of blinding.

Group 2: Low-level laser therapy (LLLT) diode LASER (650 nm, 100 mW) will be applied for 120 seconds. The laser will be applied on the first day and 48 hours after the first application. The patient will be given a placebo cream to apply five times for five days.

Group 3: Treatment with olive leaf extract (OLE). The active ingredients will be extracted from the olive leaves by the following method:
1. Dry the olive leaves in the shade, then grind them and keep them in a dark glass container
2. Extraction using 70% ethanol by ultrasound (40°C, 30 minutes)
3. Filter the extracts and then dilute them to 100 ml with distilled water
4. Determination of total phenols by the Follin-Ciocalteu method
5. Introducing the extract into a topical pharmaceutical formulation (Emulgel)

Patients are recommended to apply this preparation 5 times a day for 5 days. In addition, a placebo laser will also be applied to the site of the lesion (on the first day and after 48 hours) for blinding.

There is no follow-up after the lesion has healed.

Previous interventions:
This is a randomized controlled clinical study in which the patient sample will be divided into four equal groups according to the method of treatment used, and clinical evaluation will be conducted by blinded researchers who do not know of the type of treatment that will be used.

The sample will consist of 80 patients with recurrent herpes labialis in the vesicular stage over the age of 18 who are reviewers of the Department of Oral Medicine at Damascus University. The sample size was calculated using the G-power program.

Sample randomization:
The sample will be distributed among the four groups using an envelope containing 80 cards numbered from 1-4, where the patient takes the card corresponding to the number of the treatment group.

Methodology:
Firstly, written informed consent must first be obtained from the patient after being informed of the aims and methods of the current study. Secondly, patients will be screened to ensure they meet the inclusion criteria, then patients will be randomized into four study groups.

Interventional groups:
Group 1: Drug therapy with acyclovir: A preparation containing acyclovir at a concentration of 5% (Veramid from Medico) will be applied five times daily to the lesion site for 5 days. A placebo laser will also be applied to the site of the lesion of blinding.

Group 2: Low-level laser therapy (LLLT) diode LASER (650 nm, 100 mW) will be applied for 120 seconds. The laser will be applied on the first day and 48 hours after the first application. The patient will be given a placebo cream to apply five times for five days.

Group 3: Photodynamic therapy (PDT): The area will first be cleaned with a cotton ball soaked in a physiological solution to remove any cosmetic or sunscreen residue. Then the vesicle will be punctured with a sterile needle, to allow the discharge of the contents of the vesicle. The area will be dried using sterile gauze within the boundaries of the lesion without pressure. After that, the photosensitizer (methylene blue 0.01%) will be applied to the herpes lesion with a brush. After 5 minutes low-level level laser will be applied (Diode laser 650 nm, 100 mW). Finally, the

traces of the photosensitizer will be cleaned with a cotton ball soaked in sterile saline without pressure. The low-level laser without a photosensitizer will be applied 48 hours after the first application and the patient will be given a placebo cream to apply five times for five days.

Group 4: Treatment with olive leaf extract (OLE). The active ingredients will be extracted from the olive leaves by the following method:
1. Dry the olive leaves in the shade, then grind them and keep them in a dark glass container
2. Extraction using 70% ethanol by ultrasound (40°C, 30 minutes)
3. Filter the extracts and then dilute them to 100 ml with distilled water
4. Determination of total phenols by the Follin-Ciocalteu method
5. Introducing the extract into a topical pharmaceutical formulation (Emulgel)

Patients are recommended to apply this preparation 5 times a day for 5 days. In addition, a placebo laser will also be applied to the site of the lesion (on the first day and after 48 hours) for blinding.

There is no follow-up after the lesion has healed.

Intervention Type
Mixed

Primary outcome measure
The primary outcome measures are assessed at baseline (T0: Before taking any action in the first session) and at the following time points:
1. Pain measured using a visual analogue scale (VAS)
2. Healing speed measured using study records of the day the crust of the lesion falls off spontaneously

T1: After applying the laser (activated or placebo) in the first session
T2: The second session (after 48 hours) before applying the laser (activated or placebo)
T3: The second session after applying the laser (activated or placebo)
T4: Third session after 7 days. The day when the pain has completely disappeared is also recorded.

Secondary outcome measures
Pain measured using a VAS on day 7

Overall study start date
01/06/2021

Completion date
01/01/2024

Eligibility

Key inclusion criteria
1. Good general health
2. 18 years of age or older
3. Recurrent herpes labialis in the vesicular stage
4. Other treatments for the present lesion

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Total final enrolment
40

Key exclusion criteria
1. Pregnant and lactating
2. Patients who took antiviral drugs during the four weeks preceding treatment
3. Patients who took anti-inflammatory drugs or antibiotics during the two weeks preceding treatment
4. Diabetes
5. Patients with skin injuries that affect the course of healing or interfere with the results of the study
6. Patients who have allergic reactions to the medications used
7. Immunocompromised patients

Date of first enrolment
01/10/2021

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
Syria

Study participating centre
Damascus University
Oral Medicine Department, Faculty of Dentistry
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Sponsor information

Organisation
Damascus University

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Sponsor type
University/education

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http://www.damascusuniversity.edu.sy

ROR
https://ror.org/03m098d13

Funder(s)

Funder type
University/education

Funder Name
Damascus University

Alternative Name(s)
University of Damascus, , DU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Syria

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/02/2024

Individual participant data (IPD) sharing plan
The datasets generated and analyzed during the current study will be available on request from Mai Gaizeh Al-Hallak (memogh.1995mai@gmail.com)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			04/09/2023	No	Yes
Participant information sheet			04/09/2023	No	Yes
Participant information sheet			04/09/2023	No	Yes
Results article		20/02/2024	21/02/2024	Yes	No
Results article		02/12/2024	03/12/2024	Yes	No