ISRCTN16509838 https://doi.org/10.1186/ISRCTN16509838

The efficacy of a topical gel containing hyaluronic acid in the treatment of oral ulcers

Submission date
30/06/2020

Recruitment status
No longer recruiting

Registration date
15/07/2020

Overall study status
Completed

Last Edited
15/07/2020

Condition category
Oral Health

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Recurrent aphthous stomatitis (RAS) are common mouth ulcers. The cause of these ulcers are not always well understood, so treatment is mostly to treat the symptoms of the ulcer, to relieve pain and inflammation, and to accelerate the healing process. Medications applied directly to the ulcer have already been proved to be effective, however, more studies are needed to investigate the effectiveness of hyaluronic acid in the treatment of RAS to relieve pain and promote healing.

Most patients have their first experience of RAS between the ages of 10 and 19 years old and this may become less frequent with increasing age. Ulcers can heal spontaneously after one or two weeks but can then reoccur, this could be monthly or a few times per year.

The aim of this study is to assess the efficacy of hyaluronic-acid-based oral gel (Bexident® gel) in pain relief and ulcer healing.

Who can participate?
Candidates aged 12 to 50 years old can participate. Participants must have a current complaint of an oral ulcer (sore) that is causing pain. It's also important to not have used any other medication to treat the oral sores in the previous 48 hours, nor to suffer from other diseases that could give rise to oral sores.

What does the study involve?
Participants will be randomly allocated to relieve either the hyaluronic-acid-based oral gel (Bexident® gel), or a similar gel without hyaluronic acid. Participants will be asked to apply a gel on the sore for seven days and record the level of pain after each application according to certain instructions that will be given by the operators.

What are the possible benefits and risks of participating?
A possible benefit of using the oral gel is faster healing and pain relief. Currently, there are no known risks for the use of the oral gel.

Where is the study run from?
The Department of Biomedical, Surgical and Dental Sciences, University of Milan (Italy).

When is the study starting and how long is it expected to run for?
From November 2018 to January 2019

Who is funding the study?
The University of Milan (Italy) and BMG Pharma (Italy)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SKT_MagF_GMT.250620

Study information

Scientific Title
The efficacy of a topical gel containing hyaluronic acid in the treatment of minor recurrent aphthous ulcers in an Italian cohort: a randomized, double-blind, placebo-controlled clinical trial

Study objectives
The aim of this randomized double-blind placebo-controlled clinical trial (RCT) is to evaluate the efficacy of a Hyaluronic Acid gel for the treatment of Recurrent Aphthous Stomata in an Italian cohort.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/09/2018, the Ethical Committee of the University of Milan (Via Festa del Perdono 7, 20122, Milan, Italy; +39 (0)2503111; comitato.etico@unimi.it), ref: 44/18

Study design
Randomized double-blind placebo-controlled parallel clinical trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Recurrent aphthous stomatitis

Interventions
70 patients with the complaint of RAS will be enrolled in this study, and will be randomly be assigned to the Test or the Placebo group in an equal ratio (1:1, 35 subjects in each group). The Test group is treated with Bexident® gel (Bexident Aftas Gel®, Barcelona, ISDIN). The medicated product contains polyvinylpyrrolidone (PVP), sodium hyaluronate and a few natural

extracts. For preparation of the placebo gel, all previous ingredients are used except for PVP and sodium hyaluronate. Both formulations are packed in the same kind of tubes containing 8 ml of product.

An investigator not involved in clinical examination randomly divides and assigns a numerical code to each tube. Then the codes are assigned to patients by means of a computer-generated number list and the tubes are then given to the clinical investigators who are blind to the treatment agents contained inside.

All patients and clinical investigators are blinded to the group assignment and to the products contained in the assigned product. All the participants are clinically examined to measure the size of each ulcer at baseline, the examinations are done by the same unique investigator on all occasions (CO).

A periodontal probe are used to measure the distance between two opposite outer edges of the white margin of the ulcer. Two measurements perpendicular to each other passing through the center of the lesion are obtained and then multiplied to calculate the cross-sectional area of the ulcer. If the patient showed more than one ulcer, only the greatest one is recorded.

A visual analog scale (VAS) consisting of a 10 cm horizontal line ranking from 0 (no pain) to 10 (unbearable pain) is used for patients to self-assess their pain.

Patients are instructed, to squeeze approximately 1 milliliter of the product on a finger or a cotton tip three times a day for one week and to gently rub it on each lesion. It is recommended to refrain from eating or drinking for 60 minutes after application. For each lesion, a total amount of at least 21 ml of product is used. On the VAS scale, the patients areinstructed to mark the pain level every day before, right after, 20 and 60 minutes after drug application, from the first till the seventh day, for a total of 84 measurements for each patient.

The efficacy indices (EI) for ulcer pain are calculated at each time-point using the following formula: EI=[(Vx-V1) ÷V1] ×100%; with Vx referring to values measured within a particular time frame (in this study, at 2-7 days) and V0 referring to the baseline value to be measured at the first measurement (before the first application) on day 0. Efficacy indices (EI) are evaluated on a 4-rank scale: 1: healed, EI ≥95%; 2: marked improvement, EI ≥70% to <95%; 3: moderate improvement, EI ≥30% to <70%; 4: no improvement, EI <30%. Patients are considered to have shown marked improvement rate (MIR) when EI was ≥ 70% and improvement rate (IR) when EI was ≥ 30% (34).

Patients are also asked to report every day any adverse effects and to not use any other products for the treatment of aphthous ulcers while participating in the study or to report it (and in that case, they would be excluded from the study). The used questionnaire was dichotomic yes/no. In case of positive answer, it is asked to describe what they have experienced.

The data are then analyzed by a third operator, who is blinded to the study and does not perform any treatment on the patients. Compliance is not assessed because the total product provided to each patient was just sufficient for the designated dose and time frame of treatment.

Intervention Type
Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)
Bexident® gel (Bexident Aftas Gel®, Barcelona, ISDIN)

Primary outcome measure
Pain is measured using a visual analogue scale (VAS) at baseline, then before, right after, 20 and 60 min after drug application, three times daily, for seven days (a total of 84 measurements for each patient)

Secondary outcome measures
Change in ulcer size is measured using a periodontal probe, two measurements of the distance between the two opposite outer edges of the white margin of the ulcer perpendicular to each other passing through the center of the lesion will be obtained and then multiplied to calculate the cross-sectional area of the ulcer, at baseline, then every 24 h for 7 days

Overall study start date
01/10/2018

Completion date
30/01/2019

Eligibility

Key inclusion criteria
1. Aged between 12 and 50 years
2. Presence of at least one aphthous ulcer in an easily accessible area of the mouth and reporting pain

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
70

Total final enrolment
70

Key exclusion criteria
1. Pregnancy and lactation
2. Systemic disease such as Crohn’s disease, Behçet’s syndrome or ulcerative colitis
3. HIV, hepatitis C, or other systemic, acute or chronic infections
4. Use of other medications or drugs within 2 months, and specifically use of any local treatment for ulcers within 48 h of the start of the study

Date of first enrolment
22/10/2018

Date of final enrolment
21/12/2018

Locations

Countries of recruitment
Italy

Study participating centre
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Funder(s)

Funder type
Industry

Funder Name
BMG Pharma

Funder Name
Università degli Studi di Milano

Alternative Name(s)
Universitas Studiorum Mediolanensis, University of Milan, La Statale, UniMi

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Italy

Results and Publications

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

Intention to publish date
01/11/2020

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be included in the subsequent results publication.

IPD sharing plan summary
Other