A randomized controled trial: the effect of a medical grade honey formulation (L-Mesitran®) on clinical symptoms of recurrent vulvovaginal candidiasis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON54302

Source
ToetsingOnline

Brief title
The Honey Study

Condition

- Other condition
- Fungal infectious disorders

Synonym
Recurrent vaginal fungal infection/ Recurrent vulvovaginal candidiasis

Health condition

Vaginale infectie

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Triticum Exploitatie BV,Triticum Exploitatie BV en Vaillant fonds,Vaillant fonds

Intervention

Keyword: Candidiasis, Fluconazole, L-mesitran, Recurrent

Outcome measures

Primary outcome

The main study parameter is the vaginal culture after one month of therapy for both the treatment (L-Mesitran®) and control (Diflucan®) groups. Since the number of relapses is important for investigating the long-term efficacy, the follow-up period will be 12 months.

Secondary outcome

The secondary objectives are to investigate the effects of both treatments on the clinical symptoms, including redness, irritation, itching, dysuria, dyspareunia, vaginal discharge after 1, 6, 9, and 12 months of therapy. In addition, the prophylactic activity after 6 months maintenance therapy, and the long-term efficacy as number of relapses within 12 months will be investigated. Moreover, information about side effects, discomfort, quality of life, therapy compliance, and cost of treatments for both products will be collected and compared. Furthermore, we will analyze the vaginal microbiota (by vaginal self-swabs) to study the effect of MGH on the vaginal microenvironment.

Study description

Background summary

Recurrent vulvovaginal candidiasis (RVVC) is predicted to increase to 158 million cases annually by 2030. Treatment options are limited and in 50% of the cases relapses occur within 12 months after starting fluconazole therapy, which is the current standard of care. The pathogenesis of RVVC is multifactorial and recent studies have demonstrated that the vaginal microenvironment and activity of the immune system have a major impact on the condition. This calls for a product that meets these characteristics. Medical grade honey (MGH) has protective, antimicrobial and immunomodulatory activity and may therefore be a good alternative treatment. We postulate that MGH will actively fight ongoing infections and modulate the vaginal microenvironment by its anti-inflammatory, anti-oxidative and immunomodulatory properties, and subsequently may decrease the number of relapses when compared to fluconazole. Furthermore, we will analyze the vaginal microbiota to study the effect of MGH on the vaginal microenvironment, which may explain the possible differences in efficacy between the two groups.

Study objective

The primary objective is to investigate the vaginal culture (positive or negative) after the application of a Medical Grade Honey formulation (L-Mesitran ®) in relation to the current standard of care (Fluconazole) 1 month after starting treatment in patients with RVCC. Secondary objectives are to investigate the effects on symptoms, including redness, irritation, itching, dysuria, dyspareunia and vaginal discharge. In addition, the vaginal culture after 6 months maintenance therapy and the number of relapses within 12 months will be investigated. Moreover, information about side effects, discomfort, and quality of life will be collected and compared. Furthermore, we will analyze the vaginal microbiota (by vaginal self-swabs) to study the effect of MGH on the vaginal microenvironment.

Study design

Multi-center randomized controlled trial

Intervention

Intervention 1: Fluconazole (Diflucan®). Therapy according to manufacturer*s instructions.
As treatment for active RVVC: each patient will receive 3 capsules (150 mg), 1 capsule on day 1, 1 capsule on day 4 and 1 capsule on day 7 for acute treatment of RVVC.

As prophylaxis to prevent a new RVVC episode: once a week (150 mg) for 6 months as prophylaxis.

Intervention 2: Medical Grade Honey Formulation (L-Mesitran®)
As treatment for active RVVC - Single daily application with applicator (5 grams) for 4 weeks.
As prophylaxis to prevent a new RVVC episode: Single weekly application with applicator (5 grams) for five months.

Study burden and risks

One extra visit to the hospital, for signing informed consent and visit the farmacy. Normally, there is no long-term follow up, and patients are asked to come back when the complaints remain. Because we now want to investigate the effect on microbiological level after 1 month, 6 months and 12 months after starting treatment, we have to collect vaginal swabs. To minimize the burden to the patients, we ask the participants to take a vaginal swab themselves using a self test. These swabs need to be send by pre-paid mail to the hospital for analysis. In addition, patients will be asked to fill in a questionnaire at inclusion and 1, 6, 9, and 12 months after start therapy. The questionnaire will be sent digitally.
The investigational product L-Mesitran® is registered for the treatment of wounds and has CE and FDA certifications. No contraindications are known to date. It is advised not to use the product on patients who are sensitive to the product or any of its components or patients with allergy to honey (which is very rare and only very few cases have been reported.(1) Based on previous studies investigating the therapeutic activity of honey for the treatment of vaginitis, we do not expect any major health problems following the treatment with Medical grade honey (MGH). Two clinical studies reported that honey was safe and side effects were absent.(2, 3) Another study that compared a mixture of bee-honey and yoghurt with local tioconazole (Gynotrosyd) and reported side effects to be non-compliance (6.09%), soiling of underclothes (17%), and local irritation (1.2%).(4) During wound care, in rare occasions (less than 1%) a short burning sensation can be experienced upon application of L-Mesitran to the wounds; however, this typically disappears within a minute and may be due to the antiseptic properties, such as the osmotic activity or the low pH of MGH.
We do not expect any other side effects or discomfort to the investigational product.
No additional risks are foreseen for participation to the study. Not providing the standard care (Fluconazole) will not lead to severe complications.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Women of at least 18 years old
• Recurrent vulvovaginal candidiasis (At least 3 episodes of clinical symptoms during the last year)
• Clinical and microbiological diagnosis of (recurrent) vulvovaginal candidiasis at time of consultation
• Capacity to understand, consent, and comply with the trial procedures

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Mixed vaginal infections

• Pregnancy or the intention to become pregnant during the study period
• Women using systemic or topical antifungal medication during the last two weeks prior to inclusion
• Known allergies or containdications for Fluconazole or honey
• Candida with resistance for Fluconazole
• Women giving breastfeeding

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-08-2022
Enrollment:	252
Type:	Actual

Medical products/devices used

Generic name:	L-Mesitran soft
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	08-02-2022
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-12-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-04-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL73974.068.21