ISRCTN98567612 https://doi.org/10.1186/ISRCTN98567612

Effect of the probiotic Lactobacillus reuteri on breast inflammation and lactational mastitis

Submission date
30/03/2016

Recruitment status
Stopped

Registration date
05/04/2016

Overall study status
Stopped

Last Edited
30/08/2017

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Mastitis is a condition where a women's breast tissue becomes painful and inflamed. It is most commonly found in women who are breastfeeding, when it can be referred to as lactation mastitis. Symptoms include red, swollen areas on the breast that may feel hot and painful to touch, burning pain, a discharge from the nipples and a hard lump on the breast. Some women also have flu-like symptoms, such as a high temperature and feeling achy and tired. Mastitis is often the result of a bacterial infection. However, recent studies suggest that it is not the severity of the infection that causes symptoms and the need for antibiotic treatment but rather the inflammatory response together with pathogenic (disease-causing) or commensal ("friendly") bacteria is thought to lead to mastitis. So, is treating the condition with antibiotics the best cause of action? An alternative treatment might be to strengthen a woman's breast microbiota (the friendly bacteria usually found in the breast tissue) via probiotics, defined by the WHO as "live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host". Previous studies have shown that probiotics have reduced the number of bacteria in women suffering from mastitis. This study aims to test of a capsule containing the probiotic Lactobacillus reuteri alleviates the symptoms of lactational mastitis.

Who can participate?
Breastfeeding women aged at least 18 and suffering from mastitis.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in group 1 are given a probiotic capsule once a day for 14 days. Those in group 2 are given a placebo (dummy) capsule once a day for 14 days. All participants are asked to fill in a questionnaire, have an interview and undergo a physical examination at the start of the study. This includes the taking of a blood sample and breast milk sample. All participants are also given a symptom diary to fill in throughout the study to record their symptoms and also the behaviour of the baby. Each participant receives a phone call after 3 days in which they have an interview based on a questionnaire. After 14 days, the participants go back to the study centre and undergo the same series of tests that they had at the start of the study. They also hand in their symptom diary. All participants receive a final follow-up phone call interview based on a questionnaire on day 28.

What are the possible benefits and risks of participating?
Women eligible for this study are offered phone counseling only in clinical routine. Meeting a research midwife with special education for breastfeeding problems is a benefit of participating in the study. Lactobacillus reuteri is classified as “generally recognized as safe” by the US Food and Drug Administration. Safety and several positive health effects on adults and children (toddlers, newborn and premature babies) ingesting the probiotic Lactobacillus reuteri isolated from human breast milk have been shown in more than 80 studies.

Where is the study run from?
Sahlgrenska University Hospital, Department of Obstetrics and Gynecology (Sweden)

When is the study starting and how long is it expected to run for?
June 2015 to December 2017

Who is funding the study?
BioGaia, Stockholm (Sweden)

Who is the main contact?
Dr Verena Sengpiel

Contact information

Type(s)
Scientific

Contact name
Dr Verena Sengpiel

ORCID ID
http://orcid.org/0000-0002-3608-7430

Contact details
Department of Obstetrics and Gynecology
Sahlgrenska Academy
Sahlgrenska University Hospital
Gothenburg
Sweden
SE- 416 85

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
BioGaia CSUB0109

Study information

Scientific Title
Effect of the probiotic Lactobacillus reuteri on breast inflammation and lactational mastitis – a food supplement trial

Study objectives
1. Intake of L. reuteri will lead to faster relief in symptoms caused by breast inflammation and lactational mastitis defined as lower rating on the Kvist scale
2. Intake of L. reuteri will lead to the recovery of L. reuteri in the breast milk after 14 days treatment
3. Intake of L. reuteri will lead to lower milk counts of staphylococcus and streptococcus after 14 days treatment
4. Intake of L. reuteri will decrease the need of antibiotic treatment

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical Review Board Gothenburg, Sweden (Regionala etikprövningsnämnden i Göteborg, Sverige), 15/02/2016, ref: 1049-15

Study design
Pilot single-center double blinded randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Breast inflammation/lactational mastitis

Interventions
This is a double blind randomized placebo controlled study. Women will be randomized by blocks to receive either probiotics capsule with Lactobacillus reuteri or placebo capsules twice a day for 14 days.
At Day 1 and 14: A questionnaire based interview, physical examination and collection of blood and breast milk samples for inflammation markers, pathogen bacteria and Lactobacillus reuteri

will be performed.
Day 1-14: Symptom diary for evaluation of the mother's symptoms and baby's behavior
At Day 3 and 28: Telephone interviews based on a structured questionnaire will be assessed.

Intervention Type
Supplement

Primary outcome measure
Improvement of flu-like symptoms as experienced by study participants according to the symptoms diary, fever in °C as measured by the research midwife and local inflammation measured as scoring 0 on the Kvist scale for redness, pain and tension of the breast as well as fissures in the nipple symptoms from day 1 to 14

Secondary outcome measures
1. Inflammatory markers: concentration of C-reactive protein (CRP) and IL6 (blood and breast milk); TNFα (blood) measured day 1 and day 14
2. Infectious agents (pathogenic bacterial species count in breast milk) and identification and count of Lactobacillus reuteri in breast milk samples measured day 1 and day 14
3. Number of mothers choosing to continue breastfeeding after they have undergone an episode of breast inflammation or lactational mastitis as reported by study participants during the telephone interview on day 28
4. Symptoms in the breastfed children: agitation, sleep patterns, gastrointestinal symptoms and thrush in the mouth (which could be a complication due to maternal antibiotic treatment) as registered in the symptoms diary day 1 o 14
5. Number of women needing antibiotics treatment until day 28

Overall study start date
23/06/2015

Completion date
13/09/2016

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Women seeking help for breast inflammation and mastitis symptoms and who are counseled to home care without antibiotic treatment by health care professionals at the Department of obstetrics at Sahlgrenska University hospital. According to the hospital's routine women are recommended home care without antibiotic treatment if other not-breast-related diagnosis have been excluded, if the woman's general condition is stable and symptoms started no longer than 2-3 days before. Women with longer time since symptom debut will be offered a visit to the hospital. If the care giver after taking anamneses and examination decides that both general condition and local status allow home care without antibiotic treatment, the woman is still eligible for the study.
2. Breast inflammation/Mastitis symptoms defined as fever start ≥ 38°C before 4 hours or longer and at least 1 point for erythema and 1 point for breast tension on the "Kvist-scale" according to the research midwife's evaluation
3. Age ≥18 years

4. Capable of giving informed consent
5. Willing to comply with treatment application
6. Capable of understanding and complying with study protocol requirements
7. That the baby is considered healthy according to the routine check ups
8. Exclusive breastfeeding

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
52

Key exclusion criteria
1. Judged by a health care professional to be in need of antibiotic treatment for her breast symptoms as described above
2. Current breast injury, trauma, abscesses or other mammary pathology
3. History of/current breast cancer
4. Breast surgery in the past month
5. New pregnancy
6. Premature baby, born <37 weeks of gestational age
7. Autoimmune disease (both mother and child)
8. Known or suspected allergies to any of the components of the study product (both mother and child)
9. Participation in another investigational drug study within 30 days prior to treatment start
10. Use of any other probiotic (oral or local)
11. Ongoing antibiotic treatment

Date of first enrolment
15/02/2016

Date of final enrolment
13/09/2016

Locations

Countries of recruitment
Sweden

Study participating centre

Sahlgrenska University Hospital/Östra
Department of Obstetrics and Gynecology
Gothenburg
Sweden
416 85

Sponsor information

Organisation
Sahlgrenska University Hospital

Sponsor details
Department of Obstetrics and Gynecology
Gothenburg
Sweden
SE-41685

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04vgqjj36

Funder(s)

Funder type
Industry

Funder Name
BioGaia, Stockholm

Results and Publications

Publication and dissemination plan
Results will be published in an international peer-reviewed journal. Details to be confirmed at a later date.

Intention to publish date
30/06/2017

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available