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Chinese herbal medicine in the treatment of women with recurrent urinary tract infections

Submission date
23/10/2014

Recruitment status
No longer recruiting

Registration date
23/10/2014

Overall study status
Completed

Last Edited
06/03/2020

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
In the UK urinary tract infections (UTIs) are the most common infection that women come to the GP surgery with. About 40-50% of women experience this at least once in their lifetime. This accounts for between 1-3% of all consultations in general practice. Repeated urinary tract infections (RUTIs) are commonly defined as three episodes of UTI in the last 12 months or two episodes in the last 6 months. Between 20-30% of women who have had one episode of UTI will have a recurrent UTI, and around 25% of these will develop subsequent recurrent episodes. RUTIs can affect the quality of life, and have a high impact on healthcare costs as a result of outpatient visits, diagnostic tests and prescriptions. Whilst antibiotics are effective as a preventative treatment for RUTIs there is increasing concern about microbial resistance to these drugs and side effects of long-term use. Also, between 50-60% of women will become re-infected within 3 months after stopping antibiotics so they are not getting to the root of the problem. Chinese herbal medicine (CHM) has a long history of treating the symptoms of UTIs. In recent years there has been some encouraging research in China looking at the effect of CHM given either on its own or together with antibiotics to help prevent RUTIs. Unfortunately the methodology of most of these studies is poor and we need to conduct a more rigorous clinical study to assess the effect of CHM in preventing RUTIs. This study is the first stage of this process and will assess the feasibility of delivering CHM through GP surgeries to a group of women suffering from RUTIs. We are going to explore whether CHM helps to prevent RUTIs, whether it has any benefits in improving quality of life, and if there are any side effects from CHM treatment. We are also going to evaluate how people with RUTIs feel about taking CHM and whether it is a form of treatment that could be given by GPs or whether it needs to be given by a trained CHM practitioner.

Who can participate?
Women aged between 18-65 with three or more RUTIs in the previous 12 months.

What does the study involve?
Patients will be randomly allocated to one of four groups:
1. Active standardised CHM treatment delivered via GPs
2. Placebo standardised CHM treatment delivered via GPs
3. Active individualised treatment delivered via CHM practitioners

4. Placebo individualised treatment delivered via CHM practitioners
Standardised CHM treatment will be delivered as herbal capsules via GP practice nurses and will involve the use of fixed herbal formulae for severe episodes and for preventative treatment. These formulae will be developed through expert consultation. They will comprise of three herbs in each formula. A matching placebo (dummy) herbal capsule will be prepared and tested prior to the study. Individualised treatment will be administered by experienced practitioners of CHM and will be delivered as concentrated herbal granules that will be dissolved in hot water and drunk. Treatment will be based on the patient-specific diagnosis made by the practitioner and will vary between patients and over time.

What are the possible benefits and risks of participating?
The treatment may reduce the frequency and severity of participants RUTIs. However, this is something that has not been proven and it is the aim of this research to explore whether CHM can help in these circumstances. In CHM the herbs can cause some digestive upset like temporary nausea or loose bowels. However, these usually only lasts for 2-3 days and generally the herbs are well tolerated. In very rare instances the herbs can cause abnormal liver or kidney function. Blood tests will be conducted at the beginning of the study, after 4 weeks of taking the herbs and again at the end of the trial to measure liver and kidney function and to ensure that the participant can tolerate the Chinese herbs.

Where is the study run from?
Standardized herbal remedies administered by practice nurses will take place in Hampshire and Dorset. We anticipate that up to eight GP practices will be involved. Individualized herbs administered by CHM practitioners will take place in two complementary medicine clinics. One will be in North London and the other will be in Hove, UK. Trial participants will still require to be referred by their GPs before they can take part in this group of the study.

When is the study starting and how long is it expected to run for?
The study will run from January to December 2015.

Who is funding the study?
The National Institute of Health Research (NIHR) (UK).

Who is the main contact?
Dr Andrew Flower
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2013-004657-24

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
17290

Study information

Scientific Title
A randomised, double-blind, placebo-controlled, feasibility study exploring the role of Chinese herbal medicine in the treatment of women with recurrent urinary tract infections

Acronym
CHM for RUTIs

Study objectives
This trial is a feasibility study to provide preliminary information on:
1. The effect size of individualised, standardised and placebo Chinese herbal treatments in reducing the frequency and severity of recurrent UTIs
2. On the feasibility of administering CHM via GP practices and via non-NHS CHM practitioners and using the therapeutic environment in eliciting contextual treatment effects in the delivery of CHM

Ethics approval required
Old ethics approval format

Ethics approval(s)
Surrey Borders NRES; 17/10/2014; ref: 14/LO/1425

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
http://www.southampton.ac.uk/ruti/the_trial/forms.page

Health condition(s) or problem(s) studied
Topic: Primary Care; Subtopic: Infectious diseases and microbiology, Primary care; Disease: All Diseases

Interventions
During the trial herbal medicines will be administered either as standardised capsules or as individualised herbal granules to be dissolved in hot water to make a herbal drink.

Standardised herbs will be administered as 0.4 g capsules (four pills taken twice a day [b.d.] for preventative treatment and four pills taken four times a day [q.d.] in the event of an acute infection).

The individualised arm of the trial will follow the routine practice of CHM, which involves qualified practitioners.

Follow Up Length: 6 month(s); Study Entry : Registration and One or More Randomisations

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Current outcome measures as of 09/01/2019:
1. Symptom diaries indicating the severity of acute and recurrent UTI symptoms (reporting dysuria, haematuria, frequency during day and night, 'smelly urine', 'tummy pain', generally feeling unwell, and restriction of daily activities).
2. Rate of UTI recurrence, as reported in the symptom diaries completed for each acute UTI episode during the active phase of the trial.
3. In addition to the diary for acute UTIs participants will be asked to complete an end of month diary in which they record number of days with symptoms, changes in presentation, time lost from work, and how easy it has been to comply with the herbal medicine regime. These diaries will provide information on the rate and severity of acute infection but also on the impact of low grade, chronic infection on the lives of women. Participants will be asked to complete both an acute and a monthly diary for the 6-month follow-up of the trial to enable the evaluation of any longer term changes in infection rates.
4. Use of antibiotics for acute UTIs, elicited from symptom diaries and cross-referenced with GP notes
5. In addition we will use EQ5D, liver and renal function tests, and qualitative research.

Previous outcome measures:
1. Symptom diaries indicating the severity of acute and recurrent UTI symptoms (reporting dysuria, haematuria, frequency during day and night, 'smelly urine', 'tummy pain', generally feeling unwell, and restriction of daily activities).

2. Rate of UTI recurrence, as reported in the symptom diaries completed for each acute UTI episode during the active phase of the trial.
3. In addition to the diary for acute UTIs participants will be asked to complete an end of month diary in which they record number of days with symptoms, changes in presentation, time lost from work, and how easy it has been to comply with the herbal medicine regime. These diaries will provide information on the rate and severity of acute infection but also on the impact of low grade, chronic infection on the lives of women. Participants will be asked to complete both an acute and a monthly diary for the 6-month follow-up of the trial to enable the evaluation of any longer term changes in infection rates.
4. Use of antibiotics for acute UTIs, elicited from symptom diaries and cross-referenced with GP notes.
5. In addition we will use The Borkevic and Devilly questionnaire, MYMOP, The Morisky Medication Adherence Scale, EQ5D, liver and renal function tests, and qualitative research.

Secondary outcome measures
Not provided at time of registration

Overall study start date
05/01/2015

Completion date
30/12/2017

Eligibility

Key inclusion criteria
Women will be eligible for the trial if they are aged over 18 and under 65 years of age and have reported three or more uncomplicated recurrent lower UTIs in the previous 12 months where at least one episode has been documented as bacterial UTI.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 80; UK Sample Size: 80; Description: 80 women with a history of three infections in the previous 3 months aged between 18-65 years

Total final enrolment
61

Key exclusion criteria

Women will be excluded from the trial if they:
1. Have symptoms of complicated UTIs such as acute pyelonephritis
2. Have known hepatic or renal disease
3. Are pregnant or breastfeeding
4. Have diabetes
5. Are taking drugs which may interact with Chinese herbal medicine: cardiac glycosides (Digoxin), warfarin and lithium
6. Have psychosis, dementia or terminal illness that may prevent completion of symptom diaries.
7. Have commenced a new treatment (conventional or CAM) for RUTIs in the previous 6 months.
8. During the trial women will be excluded if they develop significantly raised liver (ALT > 90 U/l) or renal function tests (GFR < 90 mL/mm/1.73m2).
9. Any women who also become pregnant during the trial will also be advised to stop taking the CHM and to inform a member of the study team for further advice. If pregnancy is confirmed, the participant will be asked to withdraw from the intervention in the study and asked for their consent to remain for safety monitoring purposes.

Date of first enrolment
05/01/2015

Date of final enrolment
30/12/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Aldermoor Health Centre
Southampton
United Kingdom
SO16 5ST

Sponsor information

Organisation
University of Southampton (UK)

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Government

Funder Name
National Institute of Health Research (NIHR) (UK); Grant Codes: NIHR-PDF-2011-04-027

Results and Publications

Publication and dissemination plan
The clinical study report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the study. All publications will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement. The study team aim to publish in Open Access Journals.

Intention to publish date
01/09/2019

Individual participant data (IPD) sharing plan
Planned publication in a high-impact peer reviewed journal

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		07/01/2019	09/01/2019	No	No
Results article	results	28/10/2019	06/03/2020	Yes	No
HRA research summary			28/06/2023	No	No