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Alternatives to prophylactic antibiotics for the treatment of recurrent urinary tract infection in women

Submission date
18/05/2016

Recruitment status
No longer recruiting

Registration date
31/05/2016

Overall study status
Completed

Last Edited
11/05/2022

Condition category
Urological and Genital Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Most women experience infective cystitis (otherwise known as urinary tract infection or UTI) at least once in their life and some get repeated episodes which are uncomfortable and stressful; this is known as recurrent urinary tract infection (rUTI) and affects around 300,000 women each year in the UK. Giving long term low dose antibiotics is the most frequently used prevention for rUTI and although reasonably effective at suppressing the infecting bacteria, it has side effects and sometimes causes bacteria to become resistant to antibiotics. There are some alternative preventative options for rUTI that don't involve antibiotics but doctors are unsure how well they work and so tend mostly to advise antibiotics. The ALTAR trial aims to compare one such alternative non-antibiotic prevention for rUTI, a drug called methenamine hippurate, against the current standard of daily low dose antibiotic to see if the methenamine is at least as good at preventing UTI and has fewer side effects, particularly a lower chance of resistant bacteria developing.

Who can participate?
Women aged at least 18 with rUTI.

What does the study involve?
The participants are randomly allocated to one of 2 groups. Those in group 1 are given a low dose antibiotic once a day for 12 months. Those in group 2 are given methenamine hippurate, a urinary antiseptic given as a tablet, twice a day for 12-months. Each participant is followed during the 12 months that they take the UTI prevention and then for 6 months afterwards to record the benefits, side effects and costs of each treatment. They are all asked to provide urine samples at the start of their time on the study and then every 3 months until the end of their participation in the study (18 months later). If a participant suffers from a UTI during the study , they are asked to provide an additional urine sample to determine the type of bug causing the infection. Blood samples are taken at the start of the study, and then at 3 months, 6 months, 9 months and 12 months. Participants may be asked provide an additional sample at 18 months depending on the results of the previous tests. Skin swabs taken from the area near the anus are also take from each participant at the start of the study and then every 6 months until the end

of their participation in the study at 18 months. Participants are also asked to complete questionnaires on the number of infections the participants have had and what effect this has had on their general health. The questionnaires also measure the impact the infection and treatment is having on the participant's life in terms of cost and benefit. They are completed at the start of the study and at 3, 6, 9, 12, 15 and 18 months during the study. Participants are given a diary to use to keep a record of any urinary infections as they happen to make completing the questionnaires easier.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Seven NHS hospitals in the UK

When is the study starting and how long is it expected to run for?
February 2016 to November 2019

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Gillian Watson, gillian.watson@newcastle.ac.uk

Study website
https://research.ncl.ac.uk/altar/

Contact information

Type(s)
Public

Contact name
Ms Gillian Watson

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Additional identifiers

EudraCT/CTIS number
201500348736

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
20802

Study information

Scientific Title
A multicentre, pragmatic patientrandomised noninferiority trial comparing two drugs for the prevention of recurrent urinary tract infection in women both during a 12month period of use and in the subsequent 6months following completion of the prophylactic medication.

Acronym
ALTAR

Study objectives
1. To determine the relative clinical effectiveness and cost effectiveness for the NHS of two licensed preventative treatments for women with recurrent uncomplicated urinary tract infection (UTI).
2. The null hypothesis being tested is that the nonantibiotic treatment (methenamine hippurate) is inferior to the standard treatment of extended course prophylactic antibiotic for prevention of rUTI in women.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North East – Tyne & Wear South Regional Ethics Committee, 23/12/2015, ref: 15/NE/0381

Study design
Randomised; Both; Design type: Treatment, Prevention, Drug, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied

Specialty: Renal disorders, Primary sub-specialty: Renal disorders; UKCRC code/ Disease: Renal/ Noninflammatory disorders of female genital tract

Interventions
A multicentre, pragmatic patientrandomised noninferiority trial comparing two treatments for the prevention of rUTI in women during a 12month period of treatment and in the 6months following treatment completion. The standard is once daily prophylactic antibiotic, using either trimethoprim 100 mg, nitrofurantoin 50 or 100 mg depending on body weight or cefalexin 250 mg once daily for 12 months which are the recommended drugs licensed for this purpose. The choice of antibiotic will be decided by considering previous bacterial sensitivities, safety, and patient or clinician preference. The alternative
(experimental) treatment is a 1 g twice daily oral urinary antiseptic methenamine hippurate for 12 months. Participants in both arms would continue to receive treatment courses of antibiotic for UTI as needed. Apart from random allocation to either option, all participants will receive usual care including use of on demand discrete treatment antibiotic courses for UTI.

Intervention Type
Other

Primary outcome measure
1. The incidence of symptomatic antibiotic treated UTI selfreported by participants over the 12 month treatment period
2. Incremental Cost per QualityAdjusted Life Year (QALY) gained (based on responses to the Euroqol 5 dimension, 5 level (EQ5D 5L) health status questionnaire completed at baseline and 3, 6, 9 and 12 months

Secondary outcome measures
1. The occurrence of symptomatic UTI in the 6 months follow up period after stopping the allocated preventative therapy. (patient reported or clinically recorded)
2. Recorded participant antibiotic use
3. Antimicrobial resistance: Ecological change in terms of type of bacteria and their resistance patterns in isolates from i) midstream urine samples and ii) faecal reservoir (via optional rectal or perineal swabs) during the 12 month treatment period and in the 6 months following completion of treatment.
4. Number of microbiologicalproven UTIs during treatment and follow up
5. Occurrence of asymptomatic bacteriuria (ABU) during treatment and follow up
6. Hospitalisation due to UTI during treatment and follow up
7. HRQoL: Measured using the EQ5D 5L questionnaire
8. Incremental costs to the NHS, personal social services, and the patient at the end of the 12 month treatment and 18month followup phases measured using a cost-utility and a cost-benefit analysis
9. Model based estimates of costs, QALYs and net benefits over the longer terms, potentially over the patients estimated lifetime

Overall study start date
01/02/2016

Completion date
31/01/2020

Eligibility

Key inclusion criteria
1. Women aged 18 years and over
2. Women with rUTI who, in consultation with a clinician, have decided that prophylaxis is an appropriate option (to include women who have suffered at least three episodes of symptomatic UTI within the preceding 12 months or two episodes in the last 6 months or a single severe infection requiring hospitalisation)
3. Able to take a once daily oral dose of at least one of nitrofurantoin, or trimethoprim, or cephalexin
4. Able to take methenamine hippurate
5. Women who agree to take part in the trial but who are already taking Methenamine or antibiotic prophylaxis will be consented for participation and will stop their preventative therapy for a 3-month washout period. They will then be reassessed and if still eligible undergo baseline assessment and randomisation
6. Able to give informed consent for participation in trial
7. Able and willing to adhere to an 18-month study period

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 240; UK Sample Size: 240

Total final enrolment
240

Key exclusion criteria
1. Women unable to take methenamine hippurate e.g. known allergy to methenamine hippurate, severe hepatic impairment (Child–Pugh class C, score of 10 or more), gout, eGFR < 10 ml/min, Proteus sp. as consistent proven causative organism for rUTIs
2. Women who are unable to take nitrofurantoin and trimethoprim and cephalexin
3. Women with correctable urinary tract abnormalities that are considered to be contributory to the occurrence of rUTI
4. Presence of symptomatic UTI – this will be treated and symptoms resolved prior to randomisation.
5. Pregnancy or intended pregnancy in next 12 months
6. Women who are breast feeding
7. Women already taking methenamine or antibiotic prophylaxis and declining a 3-month washout period

Date of first enrolment
07/07/2016

Date of final enrolment
31/10/2017

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Cambridge University Hospital (Addenbrooks Hospital)
Hills Road
Cambridge
Cambridgeshire
United Kingdom
CB2 0QQ

Study participating centre
Central Manchester University Hospital, Manchester Royal Infirmary
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
St James University Hospital
Beckett Street
Leeds

West Yorkshire
United Kingdom
LS9 7TF

Study participating centre
NHS Greater Glasgow and Clyde
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
United Kingdom
G51 4TF

Study participating centre
Royal Liverpool & Broadgreen University Hospitals NHS Trust
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Mid Yorkshire Hospitals NHS Trust
Rowan House
Aberford Road
Wakefield
West Yorkshire
United Kingdom
WF1 4EE

Study participating centre
Pennine Acute Hospitals NHS Trust
North Manchester General Hospital
Delaunays Road
Crumpsall
Manchester
United Kingdom
M8 5RB

Sponsor information

Organisation

The Newcastle upon Tyne Hospitals NHS Foundation Trust

Sponsor details
Level 1, Regent Point
Gosforth
Newcastle Upon Tyne
England
United Kingdom
NE3 3HD

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results of the study will be presented at topic-specific national/international conferences and be published in a general medical, infectious diseases or urology themed peer-reviewed journals. The trial will provide high-level evidence to use in new or updates of existing systematic reviews such as those published by Cochrane or SIGN.

The results will be disseminated to members of professional groups such as BAUS and EAU through updates and presentations. Participants will be provided with a lay summary of results. They will also have access to a copy of journal articles through the trial website.

Intention to publish date
30/11/2020

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	09/11/2018		Yes	No
Results article		09/03/2022	11/03/2022	Yes	No
Funder report results		01/05/2022	11/05/2022	Yes	No
HRA research summary			26/07/2023	No	No