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Alternative treatments of adult female urinary tract infection

Submission date
11/02/2015

Recruitment status
No longer recruiting

Registration date
11/02/2015

Overall study status
Completed

Last Edited
29/01/2019

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Antibiotic resistance is rising and linked to prescribing in primary care (for example, by GPs). It is a national priority to try to reduce antibiotic prescribing where possible and resistance to antibiotics is a particular problem with cystitis (urinary tract infection). Cystitis in adult women is one of the most common conditions treated with antibiotics in primary care. Although the symptoms are distressing, symptoms usually settle without complications within a few days. Antibiotics do shorten the duration of symptoms and treatment is currently the norm. An alternative strategy to delay the prescription of antibiotics for a few days has been successful in respiratory (lung) infections. In cystitis this results in a modest reduction in antibiotic prescribing but slightly prolonged symptoms. It is unlikely however that the delayed prescribing strategy will be widely adopted unless an alternative approach for symptom relief is available. Two candidates for symptom relief have been identified: anti-inflammatory drugs (ibuprofen) and a herbal product (Arctostaphylos Uva ursi). This study aims to find out whether Uva ursi and/or advice to take ibuprofen would relieve the symptoms of cystitis during the period of delayed treatment. If so, the results would have the potential to change practice and to promote a delay in antibiotic prescribing in primary care, resulting in a reduction of antibiotics being prescribed.

Who can participate?
Women aged between 18 and 70, presenting to their GP with suspected cystitis

What does the study involve?
Participants are asked to accept a delayed prescription for antibiotics and then are randomly allocated into one of four groups: Group 1: Uva Ursi + advice to take ibuprofen; Group 2: Uva Ursi placebo (dummy drug) + advice to take ibuprofen; Group 3: Uva Ursi + no advice to take ibuprofen; or Group 4: Uva Ursi placebo + no advice to take ibuprofen. If their symptoms get worse or have not improved after 3-5 days participants start taking antibiotics. Severity of symptoms is recorded using a diary and the proportion of women using antibiotics in each group is measured.

What are the possible benefits and risks of participating?
It is not known whether the patients will have any personal benefit from taking part in this study. However, their participation may help to give important information about how best to

treat people with cystitis in the future. Patients would, if required, normally start taking an antibiotic prescription immediately to relieve their symptoms. In this study participants have a 1 in 4 chance of receiving no symptom relief treatment. It is possible that the uncomfortable symptoms of urinary tract infection may last longer. A prescription for antibiotics will be available should the participant wish to start taking them. Very rarely untreated urinary infection can spread to the kidneys. If this happens the participant would become more unwell and develop back pain, high fever and vomiting. A kidney infection needs urgent treatment and participants will be advise to contact their doctor if any of these symptoms develop. Also it is not known to which group participants will be allocated so it will be necessary for them to avoid taking any additional anti-inflammatories, such as Nurofen, whilst they are taking the study medication.

Where is the study run from?
University of Southampton, Southampton Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
July 2012 to May 2017

Who is funding the study?
National Institute for Health Research (UK), School of Primary Care

Who is the main contact?
Mrs Catherine Simpson

Study website
http://www.southampton.ac.uk/ctu/trialportfolio/listoftrials/atafutitrial.page?

Contact information

Type(s)
Scientific

Contact name
Mrs Catherine Simpson

Contact details
University of Southampton
Southampton Clinical Trials Unit
MailPoint 131
Tremona Road
Southampton
United Kingdom
SO16 6YD

Additional identifiers

EudraCT/CTIS number
2013-003327-11

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
3623

Study information

Scientific Title
Alternative Treatments of Adult Female Urinary Tract Infection: a double-blind, placebo-controlled, factorial randomised trial of Uva ursi and open pragmatic trial of ibuprofen

Acronym
ATAFUTI

Study objectives
Current hypothesis as of 13/09/2016:
Does Uva ursi (a herbal product) or advice to take a NSAID provide relief from urinary symptoms and reduce antibiotic use in adult women with suspected cystitis who accept the delayed prescription strategy.

Previous hypothesis:
ATAFUTI is a Phase III double blind, placebo controlled, factorial randomised trial investigating alternative treatments for adult female urinary tract infections (UTI).

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/SC/1143; First MREC approval date 22/09/2014

Study design
Randomised; Interventional and Observational; Design type: Treatment, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied

Topic: Primary Care; Subtopic: Infectious diseases and microbiology, Primary care; Disease: All Diseases

Interventions

Current interventions as of 13/09/2016:
Participants are asked to accept a delayed prescription for antibiotics and then are randomly allocated into one of four groups:
Group 1 – Uva Ursi 1200mg tds + advice to take ibuprofen
Group 2 – placebo tds + advice to take ibuprofen
Group 3 – Uva Ursi 1200mg tds + no advice to take ibuprofen
Group 4 - placebo tds + no advice to take ibuprofen.

If their symptoms get worse or have not improved after 3-5 days participants will start taking their antibiotics. Severity of symptoms is recorded using a diary and the proportion of women using antibiotics in each group measured.

Follow Up Length: 3 month(s); Study Entry : Single Randomisation only

Previous interventions:
1. Ibuprofen, 400mg tds
2. Placebo, tds
3. Uva ursi, 1200mg tds

Follow Up Length: 3 month(s); Study Entry : Single Randomisation only

Intervention Type

Drug

Phase

Phase III

Primary outcome measure

Symptom severity day 2-4 using validated diary data

Secondary outcome measures

Current secondary outcome measures as of 19/09/2016:
1. Use of antibiotics - participant records in their diary if they took the antibiotics prescribed at the time of their initial consultation.
2. Duration of moderately bad symptoms – patients record the severity of a range of urinary symptoms on a daily basis using a validated scoring system from the day of randomisation until all symptoms have resolved.
The symptoms are: fever, pain in the side, blood in urine, smelly urine, burning (burning or pain when passing urine), urgency (having to go in a hurry), day time frequency (having to go more often than usual during the day), night time frequency (having to go more often than usual during the night), tummy pain (when not passing urine), restricted activities, unwell. The scoring system is: 0 = Normal/not affected, 1 = Very little problem, 2 = Slight problem, 3 = Moderately bad, 4 = Bad, 5 = Very bad, 6 = As bad as it could be
3. Total symptom burden derived from diary data
4. Re-consultation in 1 month with UTI from notes review
5. Re-consultation in 3 months with UTI from notes review

Previous secondary outcome measures:
1. The use of antibiotics – whether the participant had to use the delayed prescription given to them by the GP at the time of their initial consultation when they were randomised to the trial. This will be recorded in their participant diary
2. Duration of moderately bad symptoms – patients record the severity of a range of urinary symptoms on a daily basis using a validated scoring system from the day of randomisation until all symptoms have resolved. The symptoms are: fever, pain in the side, blood in urine, smelly urine, burning (burning or pain when passing urine), urgency (having to go in a hurry), day time frequency (having to go more often than usual during the day), night time frequency (having to go more often than usual during the night), tummy pain (when not passing urine), restricted activities, unwell. The scoring system is: 0 = Normal/not affected, 1 = Very little problem, 2 = Slight problem, 3 = Moderately bad, 4 = Bad, 5 = Very bad, 6 = As bad as it could be
3. Re-consultation with UTI within the 3-month period following randomisation. This will be determined at the 3 months note review carried out by the GP
4. Exploratory Analysis: Differential effects on primary outcome depending on urinary culture results

Overall study start date
01/04/2015

Completion date
31/05/2017

Eligibility

Key inclusion criteria
1. Adult women (18-70) presenting to primary care with suspected lower urinary tract infection i.e. with at least one of dysuria, urgency or frequency
2. Patient able to provide informed written consent
3. Women willing to accept a delayed prescription for antibiotics

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Female

Target number of participants
Planned Sample Size: 376; UK Sample Size: 376

Key exclusion criteria

Current exclusion criteria as of 13/09/2016:
1. Known or suspected pregnancy or breast feeding. In women of child bearing age a urine pregnancy test will usually be performed unless not indicated (for instance prior hysterectomy)
2. Known immunodeficiency state, long term corticosteroids therapy or chemotherapy
3. Diabetes
4. Has any of the following known contraindications or cautions to Ibuprofen and any as listed in the current SmPC:
4.1. Asthmatics sensitive to NSAIDS/Ibuprofen or Aspirin
4.2. Severe heart failure and uncontrolled hypertension
4.3. Active gastrointestinal ulceration or bleeding
4.4. Crohn's disease or ulcerative colitis
4.5. Documented poor renal function
4.6. Chronic Kidney disease (Grade 3-5)
5. Currently or within 7 days taken antibiotics
6. Using a NSAID or Uva Ursi preparation and unwilling to discontinue for the study period
7. Suspected upper urinary tract infection (back pain, high fever>38C, systemic illness)
8. Women whom immediate antibiotics are otherwise indicated frequent recurrent infection: >3 UTI episodes in past 12 months
9. Defect of the blood clotting system
10. Bladder surgery including cystoscopy in the last four weeks
11. Currently taking Warfarin
12. Recruited to another interventional trial in previous 6 weeks

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9. Defect of the blood clotting system
10. Bladder surgery including cystoscopy in the last four weeks.
11. Currently taking Warfarin
12. Recruited to another trial in previous 4 weeks.

Date of first enrolment
01/08/2015

Date of final enrolment
21/10/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Abbeywell Surgery
United Kingdom
SO51 8QN

Study participating centre
The Adam Practice
United Kingdom
BH15 4JQ

Study participating centre
Bere Regis Surgery
United Kingdom
BH20 7HB

Study participating centre
Bosmere Medical Practice
United Kingdom
PO9 1DQ

Study participating centre
Cowplain Family Practice
United Kingdom
PO8 8DL

Study participating centre
Friarsgate Practice
United Kingdom
SO22 6EL

Study participating centre
Highcliffe Medical Centre
United Kingdom
BH23 5ET

Study participating centre
Liphook & Liss Surgery
United Kingdom
GU32 2BL

Study participating centre
Oaklands Practice
United Kingdom
GU46 7LS

Study participating centre
Portsdown Group Practice
United Kingdom
PO4 0DY

Study participating centre
Rowlands Castle Surgery
United Kingdom
PO9 6BN

Study participating centre
The Three Swans Surgery
United Kingdom
SP1 1DX

Study participating centre
Wareham Surgery
United Kingdom
BH20 4PG

Study participating centre

Woolston Lodge Surgery
United Kingdom
SO19 9AL

Study participating centre
Forest End Surgery
United Kingdom
PO7 7AH

Study participating centre
Swanage Medical Centre
United Kingdom
BH19 1HB

Study participating centre
Pioneer Medical Group
United Kingdom
BS10 6SP

Study participating centre
Brockway Medical Centre
United Kingdom
BS48 1BZ

Study participating centre
Churchdown Surgery
United Kingdom
GL3 2DB

Study participating centre
Coleridge Medical Centre
United Kingdom
EX11 1EQ

Study participating centre

Combe Down Surgery
United Kingdom
BA2 5EG

Study participating centre
Crown Medical Centre
United Kingdom
TA2 8QY

Study participating centre
Grange Road Surgery
United Kingdom
BS13 8LD

Study participating centre
Hawthorne Medical Centre
United Kingdom
SN2 1UU

Study participating centre
Kingswood Health Centre
United Kingdom
BS15 4EJ

Study participating centre
Mendip Vale Medical Practice
United Kingdom
BS49 4ER

Study participating centre
Nightingale Valley Practice
United Kingdom
BS4 4HU

Study participating centre

Portland Practice
United Kingdom
GL50 4DP

Study participating centre
Rame Group Practice
United Kingdom
PL11 2TB

Study participating centre
Rolle Medical Partnership
United Kingdom
EX8 2JF

Study participating centre
The Avenue Surgery
United Kingdom
BA12 9AA

Study participating centre
Vine Surgery
United Kingdom
BA16 0ET

Study participating centre
Wells City Practice
United Kingdom
BA5 1XJ

Study participating centre
The Wellspring Surgery
United Kingdom
BS5 9QY

Study participating centre

Westbury on Trym Primary Care Centre
United Kingdom
BS9 3AA

Study participating centre
The Boathouse Surgery
United Kingdom
RG8 7DP

Study participating centre
Bridge Street Medical Centre
United Kingdom
CB2 3LS

Study participating centre
Broadshires Health Centre
United Kingdom
OX18 1JA

Study participating centre
Brockwood Medical Practice
United Kingdom
RH3 7NJ

Study participating centre
Hightown Surgery
United Kingdom
OX16 9DB

Study participating centre
Hollow Way Medical Centre
United Kingdom
OX4 2NB

Study participating centre

The Ivers Practice
United Kingdom
SL0 9NU

Study participating centre
Kingswood Surgery,
United Kingdom
HP13 7UN

Study participating centre
Leighton Road Surgery
United Kingdom
LU7 1LB

Study participating centre
Montgomery House Surgery
United Kingdom
OX26 6HT

Study participating centre
St Clement's Surgery
United Kingdom
OX4 1JS

Study participating centre
Temple Cowley Medical Group
United Kingdom
OX4 2HL

Study participating centre
Wymondham Medical Practice
United Kingdom
NR18 0RF

Sponsor information

Organisation
University of Southampton

Sponsor details
Building 37
Highfield
Southampton
England
United Kingdom
SO17 1BJ

Sponsor type
University/education

ROR
https://ror.org/01ryk1543

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
It is intended that the results will be published in the following but there are no definite dates for this:
1. Peer-reviewed scientific journals
2. Internal report

3. Conference presentation
4. Publication on website

Intention to publish date
01/05/2017

Individual participant data (IPD) sharing plan

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?
Protocol article	protocol	08/09/2017		Yes	No
Results article	results	01/08/2019		Yes	No
HRA research summary			28/06/2023	No	No