Alternative treatments of adult female urinary tract infection

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
11/02/2015		[X] Protocol		
Registration date 11/02/2015	Overall study status Completed	Statistical analysis plan		
		[X] Results		
Last Edited 29/01/2019	Condition category Infections and Infestations	[] Individual participant data		
47/01/4017				

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

Contact information

Type(s)

Scientific

Contact name

Mrs Catherine Simpson

Contact details

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Additional identifiers

Clinical Trials Information System (CTIS) 2013-003327-11

Protocol serial number 3623

Study information

Scientific Title

Alternative Treatments of Adult Female Urinary Tract Infection: a double-blind, placebocontrolled, 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

Study type(s)

Treatment

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(s)

Symptom severity day 2-4 using validated diary data

Key secondary outcome(s))

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

Completion date

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

70 years

Sex

Female

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

Previous exclusion criteria:

- 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
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- 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

United Kingdom

England

Study participating centre Abbeywell Surgery United Kingdom SO51 8QN **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

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

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

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

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

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

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 ORF

Sponsor information

Organisation

University of Southampton

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

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?
Results article	results	01/08/2019		Yes	No
<u>Protocol article</u>	protocol	08/09/2017		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes