ISRCTN26797709 https://doi.org/10.1186/ISRCTN26797709

Community study on the effect of antibiotic use for urinary tract infections on the emergence and spread of resistance

Submission date	Recruitment status	[X] Prospectively registered
14/10/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/11/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
18/01/2019	Urological and Genital Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Stephan Harbarth

Contact details
Infection Control Program
University of Geneva Hospitals and Medical Faculty
4 Rue Gabrielle Perret-Gentil
Geneva 14
Switzerland
1211
+41 (0)22 372 9828
stephan.harbarth@hcuge.ch

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Study information

Scientific Title
A multicentre, prospective, observational cohort study on the effect of antibiotic use for urinary tract infections on the emergence and spread of antimicrobial resistance in gastrointestinal and oral commensal flora

Acronym
SATURN Workpackage 3

Study objectives
Background:
Antimicrobial resistance (AMR) is rampant among bacteria that cause healthcare- and community-acquired infections, generating additional costs and increasing the difficulty of therapeutic management. To gain a handle on the factors that are propelling the problem of AMR, molecular and patient-level investigations are necessary to better elucidate the time-varying and heterogeneous role of antibiotic selection pressure on emergence and selection of AMR.

For AMR to develop, a genetic mutation must occur or the organism must take up a resistance-conferring plasmid or DNA fragment. These mutations occur in nature, but not at a rate such that every case of AMR could be explained by a new mutation. Selective pressure exerted by antibiotics plays a central role on the acquisition, selection, persistence and transmission of resistant pathogens.

Hypothesis:
The main hypothesis to be investigated in this observational clinical cohort study is that short antibiotic treatment duration decreases the risk of carriage and transmission of antibiotic-resistant bacteria in patients treated for community-acquired urinary tract infection. More specifically, this study hypothesises that the longitudinal data provided in this cohort study and the inclusion of household members will allow to determine the effects of antibiotic treatment duration and choice of antibiotic agents (e.g. fluoroquinolones) on carriage of resistant E. coli and other clinically relevant bacteria (e.g. viridans streptococci) at the individual and household level. It is hypothesised that individuals taking longer antibiotic courses will experience a decrease of carriage of susceptible E. coli and respiratory tract commensal bacteria while on treatment, possibly increasing their subsequent risk for acquisition and selection of antibiotic-resistant bacteria. Finally, we expect differences in resistance development and impact on the commensal flora according to the initial treatment regimen.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Bioethics Committee, Medical University of Lodz approved on the 13th of July 2010 (ref: RNN /127/10/KE)
2. Medical Ethics Committee, University of Antwerp Hospital approved on the 26th of July 2010 (ref: B30020109056)
3. Internal and Community Medicine Ethics Committee, University of Geneva Hospitals approved on the 18th of August (ref: Protocole 10-123)

Study design
Prospective observational multicentre cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Urinary tract infection (UTI); antimicrobial resistance (AMR)

Interventions
Once a subject has agreed to participate and has signed the consent he/she will be asked to fill out the study questionnaire. An oral swab will be taken while the patient and, if the patient agrees, a rectal swab will be performed. The patient will be instructed on how to take a stool sample at the first defecation after the visit. These swabs will establish the subjects baseline intestinal resistance prior to the introduction of antibiotics. The household members of the subject (maximum 3) will be asked to participate in the study as well. Consenting household members will be asked to complete a survey and provide baseline stool samples and oral swabs.

All participants (index participants and household members) will be asked to provide a stool sample and oral swab:
1. on the last day of antibiotic therapy, but earliest on day five and latest on day 14 of therapy
2. twenty-eight days after the end of antibiotic treatment (28 to 43 days after initial subject entry into the study)

Antimicrobial susceptibility testing will be performed on each phenotypically distinct E. coli colony isolated. A central laboratory will perform primary cultures and susceptibility testing for stool samples, and confirmatory identification and susceptibility testing for clinical isolates. Putative E. coli colonies from stool samples will be confirmed using standard methods. Antimicrobial susceptibility to 12 antimicrobial agents will be assessed by semi-automated systems (Vitek 2, Biomerieux). Screening for ESBL-producing strains will be done on chromogenic media and using standard methodology as described in current EUCAST guidelines.

From the oral swabs, mutations in the topoisomerase genes of oral viridans group streptococci will be analyzed by sequencing the fluoroquinolone-resistant determining region (QRDR) of topoisomerase IV and DNA gyrase. Resistance mediated by efflux pumps will be detected by determination of the minimum inhibitory concentration of indicator fluoroquinolones in the absence/presence of reserpine, an efflux pump inhibitor. If new mechanisms of resistance are

found in the viridans group streptococci, they will be analyzed in detail and their ability to be transferred in S. pneumoniae after transformation will be assessed.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Carriage of antibiotic-resistant E. coli on follow-up cultures (at the end of antibiotic therapy and four weeks after the end of antibiotic therapy), stratified by duration of exposure and choice of antibiotic treatment (including also the causative pathogen of the initial episode of urinary tract infection), as well the baseline resistance prevalence of the index patient and his household members.

Secondary outcome measures
1. The impact of antibiotic therapy duration on carriage of resistant streptococci in the oropharyngeal flora
2. The proportion of susceptible bacteria on follow-up cultures

Overall study start date
01/01/2011

Completion date
31/12/2013

Eligibility

Key inclusion criteria
1. Adult patients ≥ 18 years old
2. Presenting with an acute lower or upper, uncomplicated or complicated UTI to the Emergency Room or Outpatient Clinic of the participating GP practices, clinics and hospitals
3. Requiring an antibiotic treatment of at least one dose
4. No antibiotics taken within the last 30 days
5. At least one other person living in the patient's household, defined as a person who spends at least three nights per week in the same house or apartment
6. Informed consent to the study participation

Household members (maximum 3) of the index patients will also be invited to participate.
Control patients will be recruited from patients (and their household contacts) presenting either with minor trauma or for a gynaecologic exam to the GPs / outpatient clinics.

Participant type(s)
Patient

Age group
Other

Lower age limit

18 Years

Sex
Both

Target number of participants
450 households with 2-4 participants per household (ratio of antibiotic to control households will be 4:1)

Key exclusion criteria
1. Refusal to participate
2. Unable to give informed consent
3. Presence of indwelling urinary catheters or urethral pigtail catheters
4. Renal transplant recipients; acute or chronic renal failure requiring dialysis
5. Recent discharge from hospital (during the last 30 days)
6. Treatment with systemic antibiotics within the last 30 days
7. Patients with severe sepsis or septic shock requiring intensive care
8. Permanently institutionalized residents of nursing homes or long term care facilities
9. Follow-up not possible or unlikely to be successful

Date of first enrolment
01/01/2011

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
Belgium

Poland

Switzerland

Study participating centre
Infection Control Program
Geneva 14
Switzerland
1211

Sponsor information

Organisation
University of Geneva Hospitals (Switzerland)

Sponsor details
Rue Gabrielle-Perret-Gentil 4
Geneva 14
Switzerland
1211

Sponsor type
Hospital/treatment centre

Website
http://www.hug-ge.ch/

ROR
https://ror.org/01m1pv723

Funder(s)

Funder type
Government

Funder Name
European Commission (Belgium) - DG Research (FP7-HEALTH-2009-SINGLE STAGE - N°241796)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2018	18/01/2019	Yes	No