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Use of intravenous and oral antibiotics for the treatment of skin and soft-tissue infection

Submission date
10/07/2019

Recruitment status
No longer recruiting

Registration date
11/07/2019

Overall study status
Completed

Last Edited
07/10/2022

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
Erysipelas and cellulitis, designated as skin- and soft-tissue infections (SSTI), are among the most common community-acquired infections. The incidence of SSTI is about 200 cases per 100,000 patient-years. The most common cause of SSTI is beta-haemolytic streptococci, and Staphylococcus aureus. In hospitalized patients, after initiation of intravenous therapy, antibiotic treatment may be switched to oral therapy, provided that there is a clinical response. Patients with cellulitis typically have symptomatic improvement within 24 to 48 hours of beginning antimicrobial therapy. Although, “visible” improvement of the erythema may take longer. Therefore, intravenous (IV) antibiotic treatment is frequently administered for 5 or 7 days followed by oral formulation (PO).
Aim: To investigate the treatment success of SSTIs with IV antibiotics for maximum 48 hours, followed by oral antibiotics.

Who can participate?
Adults (≥ 18 years old) presenting at the Spital Emmental with the diagnosis of SSTI.

What does the study involve?
Patients with SSTI that are on intravenous treatment with antibiotics and who fulfil clinical criteria according to a predefined checklist will be switched to oral antibiotics after 48 hours. Patients who do not fulfil the criteria will remain on original treatment.

What are the possible benefits and risks of participating?
The possible benefits are removal of intravenous lines and early discharge from the hospital. The possible risks are relapse of infection because of insufficient bioavailability of the antibiotic compound. Early switch from IV to PO antibiotic therapy may be a substantial benefit for both the patient and the health care system.

Where is the study run from?
Department of Internal Medicine in two hospitals (Burgdorf and Langnau) belonging to the Spital Emmental (Canton Bern).

When is the study starting and how long is it expected to run for?
August 2019 to December 2020

Who is funding the study?
Investigator-initiated and funded

Who is the main contact?
Prof. Parham Sendi
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2019-00558

Study information

Scientific Title
Spital Emmental Skin and Soft-Tissue Infection Pilot Study

Acronym

SE-SSTI

Study objectives
Intravenous antibiotic therapy for maximum 48 hours followed by oral formulation of antibiotic therapy (further designated as intervention arm) has the same clinical cure rate in SSTIs as
1. A control group for comparison (duration of intravenous therapy not restricted and decided at the discretion of treating team, further designated as observation arm)
and
2. That reported in the literature for SSTIs (85% - 90%).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/07/2019, Cantonal Ethical Committee Bern (Kantonale Ethikkommission für die Forschung
Murtenstrasse 31, 3010, Bern, Switzerland; +41 31 633 70 70; info.kek.kapa@gef.be.ch), ref: 2019-00558

Study design
Prospective non-randomised clinical trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

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
Skin- and soft-tissue Infection (SSTI)

Interventions
The planned intervention is the switch from intravenous to oral antibiotic treatment after 48 hours, provided that clinical criteria according to a predefined checklist are fulfilled (designated as intervention arm). Hence, there will be an “intervention arm” and an “observation arm.”
Antibiotics used:

Intervention Type
Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
Amoxicillin/Clavulante or Clindamycin oral in the intervention arm. Amoxicililn/Clavulante or Cefuroxime intravenous in the control arm.

Primary outcome measure
The number cured cases measured as ‘total number of treated cases’ minus ‘the number of failed cases’. Clinical failure is defined as increase in symptoms during antibiotic treatment or new course of antibiotics between end of therapy and 2 weeks after end of treatment or death or readmission for skin and soft tissue infection within 30 days of discharge.

Secondary outcome measures
1. Duration of intravenous treatment measured in number of doses and days of treatment assessed by reviewing patient notes.
2. The following baseline factors and parameters will be assessed at baseline and during treatment, respectively:
2.1 Host variables: Age, sex, body mass index, allergies, comorbidities (cardiovascular), renal function, diabetes mellitus, insulin dependent, immunosuppression, cancer, alcohol consumption, IVDU.*
2.2 Clinical sepsis variables: pain at the site of infection, the presence of chills, body temperature, blood pressure (diastolic and systolic), heart frequency, O2-Saturation with or without oxygen.*
2.3 Referral dynamic variables: time from onset of symptoms to first physician contact, time from first physician contact to referral.*
2.4 SSTI variables: site of infection, size, color, portal of entrance, blisters*
2.5 Laboratory values (only if available and obtained at the discretion of the treating team): Hemoglobin, leukocytes, thrombocytes, creatinine, urea, ASAT, ALAT, bilirubin, alkaline phosphatase.^
2.6 Bacterial variables: Microorganism, minimal inhibitory concentration of antimicrobial compounds.*
2.7 Antibiotic variables: compound, dose, dosing scheme, application form, duration of treatment.*
*Assessed by reviewing patient notes.
^Laboratory investigations are ordered at the discretion of the treating physician. However, laboratory results will be obtained for the study, alongside to the closest date of clinical data.
3. Clinical recovery assessed by a short telephone interview at day 30.

Overall study start date
01/02/2019

Completion date
01/08/2021

Eligibility

Key inclusion criteria
1. Adult (≥ 18 years old) with SSTI
2. Ability to understand and sign patient consent form
3. Ability to consent for data use, or to consent for oral treatment, or to consent for both
4. Not fulfilling exclusion criteria

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Total number of participants: As this is a pilot study, we target 50 patients in the intervention arm. In addition, we aim to observe 50 patients without structured switch from intravenous to oral antibiotics for comparison (observation arm).

Total final enrolment
97

Key exclusion criteria
1. Received antibiotics 14 days or less prior to study inclusion
2. Necrotizing fasciitis
3. Septic shock or infection requiring intensive medicine care
4. Impetigo without erysipelas or cellulitis
5. Arthritis, Osteomyelitis, Tenosynovitis, Prosthetic Joint Infection, Foreign Body Infection
6. Mastitis
7. Non-bacterial infection or sterile skin inflammation
8. Surgical site infections
9. Skin abscess, bursitis,
10. Diabetic Foot Infection PEDIS classification 3
11. Bacteraemia with Staphylococcus aureus or Pseudomonas aeruginosa
12. Ecthyma gangraenosum
13. Gram-negative bacteria as causing organism for SSTI
14. Pregnant and lactating women can be included ONLY in the observation arm, and NOT in the intervention arm.

Date of first enrolment
15/07/2019

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
Switzerland

Study participating centre
Spital Emmental, Medizinische Klinik
Dorfbergstr. 10
Langnau
Switzerland
3550

Study participating centre
Spital Emmental, Medizinische Klinik
Oberburgstrasse 54
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3400

Sponsor information

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Sponsor type
University/education

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ROR
https://ror.org/02k7v4d05

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Presentation at scientific congresses in Spring 2021
Publication in peer reviewed international Journal in Summer 2021

Intention to publish date
01/08/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Data will be entered in a coded fashion in RedCap and stored at the server of the CTU Bern, Switzerland. Bacteria isolated from the patient and responsible for the SSTI will be stored with labelled code at the Institute for Infectious Diseases of the University of Bern in a freezer at -80° C. The patient material alongside the bacteria will be stored. The labelling of the bacteria corresponds to the patient code for this study. Project data is recorded with an electronic Case Report Form via Redcap®. The list of the source data used in the project includes CODED original records from the patient charts, clinical findings, observations and laboratory values (all outlined in 2.2), as well as patient responses from interviews in direct conversation (personal or telephone). All collected data are collected during the daily practice, also.
Data handling and record keeping / archiving / Data Management System (Hardware and software):
The CRFs in this trial are implemented electronically using a dedicated electronic data capturing (EDC) system (REDCap, https://www.project-redcap.org/). The EDC system is activated for the trial only after successfully passing a formal test procedure. All data entered in the CRFs are stored on a Linux server in a dedicated mySQL database.
Responsibility for hosting the EDC system and the database lies with CTU Bern.
Confidentiality and coding:
Trial and participant data will be handled with uttermost discretion and is only accessible to authorised personnel who require the data to fulfil their duties within the scope of the study. On the CRFs and other study specific documents, participants are only identified by a unique participant number. The server hosting the EDC system and the database is kept in a locked server-room. Only the system administrators have direct access to the server and back-up tapes. A role concept with personal passwords (site investigator, statistician, monitor, administrator etc.) regulates permission for each user to use the system and database as he/she requires.
All data entered into the CRFs are transferred to the database using Transport Layer Security (TLS) encryption. Each data point has attributes attached to it identifying the user who entered it with the exact time and date. Retrospective alterations of data in the database are recorded in an audit table. Time, table, data field and altered value, and the person are recorded (audit trail).
A multi-level back-up system is implemented. Back-ups of the whole system including the database are run internally several times per day and on external tapes once a day. The back-up tapes are stored in a secure place in a different building.
Coding/Pseudonymization:
e.g. Langnau patients 1-01, 1-02, 1-03, … / Burgdorf patients 2-01, 2-02, 2-03, …

Study-related data of the patient will be collected in a coded manner. The names of the patients will not be disclosed. A code (unique, consecutive numbered per center) will be attributed to each patient registered.
The Key List / Random List:
The code key list is kept in a locked cupboard at the secretary room of internal medicine. Members of the study team will not have access to the key (except PIs). One list for each site (Burgdorf and Langnau) will be generated.Retention and destruction of study data and biological material
Archiving and Destruction (Analysis and archiving):
At final analyses, data files will be extracted from the database into statistical packages to be analyzed. After database lock, the status of the database is recorded in special archive tables. The sponsor will keep the Trial Master File, the extracted data, the meta data and interim/final reports for at least 10 years.
Electronic and Central Data Validation:
Data is checked by the EDC system for completeness and plausibility. Furthermore, selected data points are cross-checked for plausibility with previously entered data for that participant. In addition, central data reviews will be performed on a regular basis to ensure completeness of the data collected and accuracy of the primary outcome data.
Before database lock the PI will validate the collected data with his signature.
Biological Material:
No biological 'host' material from the patient will be stored. Isolated bacteria will be stored at the IFIK of the University of Bern at -80°C under SOP accredited regulations for 10 years.
The study data and bacteria may be used for a study in the future (further use). In such a scenario, approval from the corresponding EC will be requested prior to the start of the study.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		12/04/2022	08/07/2022	Yes	No
Protocol file	version 4.1	18/11/2019	07/10/2022	No	No