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Quality control of antibiotic stewardship

Submission date
09/02/2022

Recruitment status
No longer recruiting

Registration date
16/06/2022

Overall study status
Completed

Last Edited
04/12/2024

Condition category
Respiratory

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Pneumonia is a leading cause of illness and death worldwide. It can be categorized into two main groups as community-acquired (CAP) or hospital-acquired (HAP), with HAP being defined as pneumonia occurring 48 hours or more after hospitalisation. Clinical presentation cannot distinguish between the wide variety of causes. One of the most important prognostic factors in pneumonia is early and adequate antibiotic treatment. Therefore, initial empirical antibiotic treatment is chosen to cover the suspected range of bacteria. Identification of the causative agent is pivotal to adjusting the empirical antibiotic treatment to targeted treatment, a primary goal of antimicrobial stewardship. Antimicrobial stewardship targets the best clinical outcomes while keeping unnecessary or inappropriate antibiotic use to a minimum in order to decrease side effects, reduce the emergence of resistance and for cost-effectiveness purposes. Optimal antibiotic treatment includes escalation or de-escalation according to microbiological results, discontinuation and taking allergies into account, whereas inappropriate therapy is empirical therapy in discordance with susceptibility testing, without clinical response or with a too broad a spectrum for the identified pathogen. The aim of this study is to evaluate whether a rapid multiplex polymerase chain reaction (PCR) testing of the bronchoalveolar lavage (BAL) can decrease the time on inappropriate antimicrobial treatment in patients with a lower respiratory tract infection compared to conventional microbiological tests alone. BAL is a procedure in which a bronchoscope is passed through the mouth or nose into the lungs and fluid is squirted into a small part of the lung and then recollected for analysis.

Who can participate?
Patients aged 18 years in hospital undergoing bronchoscopy for respiratory tract infection

What does the study involve?
Participants will be randomly allocated to BAL culture or BAL culture and PCR. Antibiotic treatment will be assessed based on microbiology/PCR results. The follow-up period encompasses the whole duration of hospitalization up to a maximum of 30 days.

What are the possible benefits and risks of participating?
Routine microbiologic testing methods to identify the causative agent are culture-based and results take 48 to 72 hours. In addition to the time delay, they are not suitable to detect atypical pathogens. The yield of sputum cultures is variable, generally low and influenced by several factors such as specimen collection, transport, time of processing, and previous antibiotic

treatment with the highest yield in patients before the start of antibiotic treatment. BAL has a higher yield than sputum culture, and is of additional value in identifying the causative agent, especially in patients without sputum production and those non-responsive to empirical treatment. However, in patients already receiving antibiotic treatment the diagnostic yield in BAL is also reduced. With multiplex PCR methods, the rate of pathogen detection can be improved significantly, especially in antibiotic exposed patients, with the potential to enable targeted treatment.

Where is the study run from?
1. University Hospital Basel (Switzerland)
2. Universitätsklinikum Freiburg (Germany)

When is the study starting and how long is it expected to run for?
January 2021 to January 2024

Who is funding the study?
University Hospital Basel (Switzerland)

Who is the main contact?
Prof. Daiana Stolz
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Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
V2

Study information

Scientific Title
Quality control of antibiotic stewardship

Acronym
Flagship IV

Study objectives
The purpose of this quality control project is to evaluate whether a rapid multiplex PCR of the bronchoalveolar lavage (BAL) can decrease time on inappropriate antimicrobial therapy in patients with lower respiratory tract infection (LRTI) compared to conventional microbiological investigations alone as used in the clinical routine of a tertiary care institution.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/04/2021, Ethikkommission Nordwest- und Zentralschweiz (EKNZ, Hebelstrasse 53, 4056 Basel, Switzerland; +41 (0)612681350; eknz@bs.ch), ref: 2021-00451

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Lower respiratory tract infection (LRTI)

Interventions
The BIOFIRE® FILMARRAY® Pneumonia plus Panel tests for 18 bacteria (11 Gram-negative, 4 Gram-positive and 3 atypical), 7 antibiotic resistance markers, and 9 viruses that cause pneumonia and other lower respiratory tract infections. It offers an overall sensitivity and specificity for BAL-like samples of 96,2% and 98.3%, respectively. The Biofire Pneumonia Panel is run on the BIOFIRE® FILMARRAY® System, a US FDA, CE-IVD, and TGA certified multiplex PCR system. The system integrates sample preparation, nucleic acid extraction and purification, amplification, detection and analysis into one simple system that requires just 2 minutes of hands-on time, with a total run time of about 75 to 90 minutes.

The new panel complements the existing BIOFIRE® FILMARRAY® Respiratory Panel 2+ to provide a comprehensive diagnostic tool for pneumonia and other lower respiratory tract infections. Rapid and accurate identification of the causative agent of both community and health-care associated respiratory tract infections can help improve patient management through timely and effective antimicrobial therapy. A rapid diagnosis can assist with directing appropriate infection control practices thereby aiding in the prevention of the secondary spread of infection, shortening hospital stays, reducing ancillary testing, and reducing overall health care costs. The disposable cartridge is compatible with standard waste disposal procedures of hospitals and laboratories.

Hospitalized patients undergoing bronchoscopy for respiratory tract infection will be randomized to BAL culture or BAL culture and PCR. Antibiotic therapy will be assessed based on microbiology/PCR results. The follow-up period encompasses the whole duration of hospitalization up to a maximum of 30 days.

Intervention Type
Other

Primary outcome(s)
Time on inappropriate therapy in hours, recorded daily up to a total of 30 days, defined as anti-microbial therapy:
1. With no identifiable pathogen or
2. Not active according to in-vitro susceptibility testing of the identified pathogen or
3. With known intrinsic resistance of the identified pathogen to the given therapy or
4. Having a spectrum too broad for the identified pathogen (antimicrobial therapy considered broad when switching to a different antimicrobial therapy with a narrower spectrum continues to show a favourable clinical course) and in the case where there is a lack of evidence suggesting resistance of the microorganism to a narrower antimicrobial therapy or
5. Continuation of the antimicrobial therapy beyond the guideline-suggested duration e.g. for pneumonia 5 to 7 days

Key secondary outcome(s))
Clinical outcomes measured using patients' medical records daily up to a total of 30 days:
1. Time to clinical stability (in hours)
2. Length of hospital stay (in hours)
3. Mortality
4. Adverse events

Completion date
31/01/2024

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Clinical indication for diagnostic bronchoscopy with bronchoalveolar lavage
3. Suspicion of lower respiratory tract infection – in immunocompetent patients infiltrate must be confirmed; in immunocompromised patients an infiltrate is not required
4. Evidence of systemic inflammation (such as abnormal white blood cell count – either leukocytosis (>10.0x10e9/l) or leukopenia (<4.0x10e9/l) – or C-reactive protein (CRP) or procalcitonin (PCT) values above the local upper limit

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Ambulatory patients
2. Patients intubated at the time of inclusion
3. Neutropenic patients as defined by neutrophils <0.5x10e9/l
4. Haemodynamic instability or signs of life-threatening infection precluding a narrowing of antimicrobial therapy
5. Prior enrolment in an intervention study within the last 30 days
6. Women who are pregnant or breastfeeding

Date of first enrolment
01/02/2022

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
Germany

Switzerland

Study participating centre
University Hospital Basel
Clinic of Pneumology and Respiratory Cell Research
Petersgraben 4
Basel
Switzerland
4031

Study participating centre
Universitätsklinikum Freiburg, Klinik für Pneumologie
Kilianstrasse 5
Freiburg im Breisgau
Germany
79106

Sponsor information

Organisation
University Hospital of Basel

ROR
https://ror.org/04k51q396

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Universitätsspital Basel

Alternative Name(s)
University Hospital Basel, University Hospital of Basel, The University Hospital Basel, Hôpital Universitaire de Bâle, L'Hôpital universitaire de Bâle, Das Universitätsspital Basel, UHB

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location

Switzerland

Results and Publications

Individual participant data (IPD) sharing plan

Due to technical incompatibilities the researchers don’t expect the dataset to be made available. Data will be stored at the University Hospital Basel.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.0	16/09/2022	17/03/2023	No	No