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Blood Stream Infection: Focus On Outcomes - An observational study in patients with blood stream infections

Submission date
23/05/2013

Recruitment status
No longer recruiting

Registration date
08/10/2013

Overall study status
Completed

Last Edited
26/09/2016

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
We are carrying out a study on 2,000 patients to look at what happens to them after they contract a blood stream infection with one of five different bacteria or fungi known to cause serious infection. We hope to identify factors that we could modify to improve what happens to similar patients in the future. There is some evidence from small studies that giving the right antibiotics as soon as possible and removing the source of infection where possible will benefit patients with this disease. This study aims to look at much larger numbers of patients in five different centres to be more certain of what things we need to change in the management of patients with blood stream infections to make a beneficial difference to what happens.

Who can participate?
All patients at the five participating sites (Newcastle, Leeds, Cardiff, London and Bristol) with a blood stream infection from one of the five types of bacteria and fungi we are studying will be recruited to the study.

What does the study involve?
Over a period of two years, extensive clinical data will be collected on the patients to look in depth at things that might affect outcome. This will include information such as the disease the patient came to the hospital with, from where they were admitted to the hospital, the ward the patient stayed on, staffing levels on the ward, and how quickly they received the correct antibiotics for their infection.
At the end of the study, once all the data has been collected it will be analysed to see what factors made a difference to how well the patients did; for example, how quickly they responded to treatment and left hospital. As a result of this analysis, we will develop a set of guidelines for doctors treating patients with blood stream infections to enable them to give patients with this type of infection the best possible care to aid their recovery.

What are the possible benefits and risks of participating?
There will be no immediate direct benefit to those taking part but there should be benefits to future patients who get a blood stream infection as we will have identified the best

management for these patients. This is an observational study and those taking part will not be asked to do anything extra.

Where is the study run from?
The study has been set up by the Department of Medical Microbiology in North Bristol NHS Trust. There are five participating sites in the UK: Newcastle, Leeds, Cardiff, London and Bristol

When is the study starting and how long is it expected to run for?
The recruitment started at the end of 2010. Participants were enrolled on the study for a period of two years.

Who is funding the study?
National Institute for Health Research, UK.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
PGfAR RP-PG-0707-10043

Study information

Scientific Title

Blood Stream Infection: Focus On Outcomes: A multicentre prospective observational study in patients with blood stream infections

Acronym
BSIFOO

Study objectives
Blood Stream Infection (BSI) has been chosen for study because it is common, the aetiological pathogen is clear, it has a significant mortality and there are no specific NHS data on outcomes or factors associated with poor outcome. The aim of the proposed work is to identify remediable risk factors that influence outcome in BSI due to the following pathogens MRSA, MSSA, ESBL-producing E. coli/Klebsiella spp, Non ESBL-producing E. coli, P. aeruginosa and Candida spp

Risk factors for mortality in BSI due to MRSA, ESBL-producing E. coli /Klebsiella spp, P. aeruginosa and Candida spp have been studied mainly in single-centre retrospective cohort studies performed either in North America or the Far East. Their relevance and generalisability for the NHS is therefore limited. A number of patient factors are known to be associated with adverse outcomes, for example, severe sepsis, abdominal infection, neutropaenia, increasing Acute Physiology and Chronic Health Evaluation II (APACHE II) score, diabetes mellitus, ICU location, unknown primary focus of infection, organ failures, circulatory shock and pneumonia.

In contrast, timely appropriate antimicrobial chemotherapy and removal of infected prosthetic materials, especially intravenous (iv) lines, are thought to be beneficial from the single-centre studies, but this far no multi-centre studies have been undertaken to confirm their importance in the UK, estimate the size of their effect or to identify other factors that can be modified to improve outcome. Factors related to antibiotic activity and drug pharmacokinetics that impact beneficially on outcome, include effective definitive antibiotic therapy, for example; the use of carbapenems for infections with ESBLs and the aminoglycoside or fluoroquinolone peak serum concentration to MIC ratio in P. aeruginosa infections. In infections with MRSA outcome can be influenced by the vancomycin serum AUC/MIC ratio, poor cidality and the presence of the agr II gene (MRSA). The impact of early (empirical) antibiotic therapy in improving outcome is controversial, the evidence being conflicting for the Gram-negative pathogens (E. coli /Klebsiella spp) especially. Although not studied in infection outcomes, it is known that nurse staffing levels can affect patient mortality in general and the intervention of medical infection specialists can improve outcomes in BSI specifically.

It is envisaged that the study will identify modifiable risk factors for poor outcome in the patients with BSI to enable a BSI care bundle to be developed for the NHS to improve outcome for this patient group. Care bundles are a structured way of improving processes of care and patient outcomes. In general these are a small straightforward set of practices - usually three to five - that, when performed collectively, reliably and continuously, have been proven to improve patient outcomes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES South West 4 REC, 15/09/2010, ref: 10/H0102/51

Study design
Multicentre prospective observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Blood Stream Infections

Interventions
The study will be of a prospective cohort design and will involve the collection of data from each of the five centres Newcastle, Leeds, Cardiff, London and Bristol, to generate a large clinical library of information surrounding outcome of infection with one of the following pathogens: MRSA, MSSA, ESBL-producing E. coli/ Klebsiella spp., non ESBL-producing E. coli, P. aeruginosa and Candida spp.

Over a two-year period all patients from the five sites who have BSI associated with one of the key pathogens will be included in the main study and the relevant data items collected. This is an observational study so no extra investigation, procedures or interventions will take place. Only routine investigations or tests will be performed and recorded in the patient records as usual.

Following laboratory diagnosis of a BSI with one of the relevant pathogens named above, the research nurse will record patient data from the patient records and laboratory computer system. Specific data will be collected on the risk factors associated with all causes of death in patients for a maximum period of 28 days following the diagnosis of the BSI. In order to exclude selection bias, data will be collected from consecutive patients at each site who fulfil the inclusion/exclusion criteria. Where available some data items will be collected for the period leading up to the diagnosis of the BSI. Data on the care environment will be collected from one day before diagnosis of the BSI to discharge or day 7. Microbiological data will also be recorded for each organism.

All isolates from each centre will be sent to the central laboratory. Antibiotic susceptibility will be determined in the central laboratory. The appropriateness of the antibiotic therapy will be assessed based on the dosing regime of the antibiotic and the susceptibility of the organism to the therapeutic regimen.

The data collected at each site will be entered onto a web-based system to be uploaded centrally into a database. All data will be encrypted before sending. Before the central database is released for statistical analysis it will be anonymised. Following release of the database, statistical analysis as described in section nine will be undertaken to identify the modifiable risks for poor outcome.

Screening Data
Each site will process all samples for blood culture by their standard laboratory method for culturing blood for Blood Stream Infections. The hospital laboratory computer systems will then be searched on a daily basis to identify all blood cultures that are positive for a blood stream infection. Following identification of a Blood Stream Infection a basic set of data items will be collected. This will enable the identification of which subsequent data sets should be collected.

Patient Information Data
For patients with Blood Stream Infections with one of the key pathogens two main data sets will have to be recorded. One set of information will need to be recorded once and two sets will need to be recorded sequentially These data items will be collected from different sources including the Hospital Patient Administration System (PAS), the Hospital Laboratory System (LIMS) and the patient notes.

Care Environment Data
For patients with Blood Stream Infections with one of the key pathogens care environment data set will be obtained. These data items will be collected at ward level.

Treatment and Microbiological Data
All antimicrobials administered will be noted including the time and date of first and last administration, route and dose. The time from initial blood culture sampling to appropriate antibiotic administration time will be calculated, as will the duration of appropriate therapy.

Appropriate antimicrobial chemotherapy will be defined as: at least one drug to which the pathogen susceptible in a phenotypic test system to be administered for >36 hrs. For vancomycin and aminoglycoside therapy, serum concentrations will be recorded and therapeutic drug monitoring will be defined as satisfactory or not by reference to local guidelines.

A population pharmacokinetic model will be built for both vancomycin and aminoglycosides to allow the magnitude of pharmacodynamic drivers of outcome for these agents to be established in the patient population. That is AUC/MIC for vancomycin and Cmax or AUC/MIC for aminoglycosides.

Antibiotic resistance will be defined by the European Committee on Antimicrobial Susceptibility Testing (www.eucast.org) clinical breakpoints. For ESBL producers the ESBL type will be established by microarray. For S. aureus isolates, the vancomycin MIC by Etest, population analysis profile, presence of agr II gene, bactericidal activity of vancomycin against the strain (log kill at 72h) will be determined. Candida species will be identified to species level, MIC tests performed by micro broth dilution to the therapies given. For P. aeruginosa, after MIC determination, the resistance mechanism will be established for all non wild type isolates. P. aeruginosa and ESBL producers will be typed.

Where the definitions of appropriate and inappropriate antibiotic therapy are controversial, they will be decided by consensus among the Centre lead investigators and the PI, who will be blinded as to the outcome. The panel of the investigators will employ the Delphi technique, which is a method for generating information about a likely outcome involving a number of iterative stages through which expert opinions take a consensual view of what might happen.

Intervention Type
Other

Phase

Not Applicable

Primary outcome measure
All-cause mortality and time to death (up to 28 days from when the blood samples was taken)

Secondary outcome measures
1. Resolution of fever (temperature <=37.5°C for >=48 hours) and time to resolution of fever (up to 28 days from when the blood samples was taken)
2. Discharge from hospital and time to discharge (up to 28 days from when the blood samples was taken)
3. C. difficile infection (up to 28 days from when the blood samples was taken)

Overall study start date
01/10/2010

Completion date
30/09/2013

Eligibility

Key inclusion criteria
1. Age 18 years of age and over
2. Blood Stream Infection with one of the key pathogens plus Centres of Disease Control criteria for infection in the urinary tract, surgical site, pneumonia, blood stream, bone and joint, central nervous system, cardiovascular system, ENT, gastrointestinal system, reproductive system, skin and skin structure, infection or disseminated infection.
3. Blood Stream Infection with any other organism for collection of the limited data set

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
2635

Key exclusion criteria
1. Less than 18 years of age
2. Having cystic fibrosis
3. Having disease associated with human immunodeficiency virus
4. Patients on the end of care pathway
5. Duplicate organism (same organism within 14 days of previous blood culture)
6. Prisoners or young offenders in the custody of HM Prison Service in England or Wales

Date of first enrolment
01/10/2010

Date of final enrolment
30/09/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
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Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (NIHR) (UK) Program Grant PGfAR RP-PG-0707-10043

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