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Analysis of geNe Expression and bioMarkers fOr poiNt-of-care dEcision support in Sepsis

Submission date
10/10/2013

Recruitment status
No longer recruiting

Registration date
28/02/2014

Overall study status
Completed

Last Edited
21/02/2017

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
Sepsis is a potentially life-threatening condition caused by a severe infection. When someone develops sepsis, inflammation occurs not just at the site of the infection but throughout the body. This widespread inflammation can be very harmful. Similar problems arise after cardiac arrest. Currently, the diagnosis of sepsis relies on time-consuming and insufficient microbial culture and assessment of blood proteins. There is a clear clinical need for a timely and accurate medical diagnosis. We will be looking in detail at proteins and genetic information that we suspect may help doctors to differentiate between patients with different type of infections and inflammation.

Who can participate?
We are recruiting a number of people with severe infections causing organ failure (also known as severe sepsis and septic shock) or who have suffered cardiac arrest.

What does the study involve?
In total, we will take 94 ml (about nine tablespoonfuls) of blood in addition to the blood tests that have been taken as part of normal care. We would also like to send a short questionnaire after 6 months to find out how the patients are doing. The questionnaire will take about 20 minutes to fill in.

What are the possible benefits and risks of participating?
There will be no benefit to the patients in taking part. It is unlikely that the extra blood samples could cause any harm because the volume of blood taken is small. The blood samples are taken out of one of the lines that are already in place as part of routine care there are no extra needles.

Where is the study run from?
Cardiff University (UK).

When is study starting and how long is it expected to run for?
The study started in March 2013 and will run until July 2014.

Who is funding the study?
The Technology Strategy Board (UK).

Who is the main contact?
Prof Judith E Hall OBE
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
1.0

Study information

Scientific Title
Analysis of geNe Expression and bioMarkers fOr poiNt-of-care dEcision support in Sepsis: a prospective observational study

Acronym
ANEMONES

Study objectives
This project will use two different approaches (a) genetic and (b) multiple protein assays to validate novel inflammatory or sepsis-associated markers identified by very complex statistics developed by Nottingham Trent University. This will enable us to differentiate between features specific to infection and those that are common to severe inflammation. The project will identify highly significant biological markers that will help us to rapidly diagnose sepsis early in the disease and differentiate it from severe inflammation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Wales Research Ethics Committee Panel D; Ref: 12/WA/0303

Primary study design
Observational

Study design
Prospective observational study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Sepsis, SIRS without infection

Interventions
We will study two patient groups: patients with severe sepsis from abdominal and pulmonary disease (n=160), and a positive control group. The positive control group will be patients with inflammation and organ failure not related to infection (n=40) and for this we will include patients admitted to the Intensive Care after out of hospital cardiac arrest.

The following blood samples will be taken from ICU patients with organ failure (all subjects):

5 ml heparinised blood frozen on days 1, 2, 5 and discharge for DNA micro-arrays and purification of PBLs
1 ml heparinised blood frozen on days 1, 2, 5 and discharge for storage
3 x heparinised 1.0 ml blood for platform development
2 ml EDTA blood on day 1 for CMV serology
2 ml EDTA blood on day 5 for CMV PCR
2 ml EDTA blood on day 1 for 16S PCR
7 ml clotted blood on day 1, day 2, day 5 and day of discharge for purification of serum and cytokine/protein biomarker analysis
6 ml EDTA blood on day 1, day 2, day 5 and day of discharge for purification of plasma and cytokine/protein biomarker analysis

The samples taken will undergo the following tests: 16S PCR, microarray analysis, qPCR analysis, proteomic analysis

Clinical data describing in detail the progress and severity of illness will be imported from the ICU clinical databases. Data items recorded will include physiological and routine laboratory variables. We will collect the following microbiology data:
Results of positive microbiology cultures including:
The date the sample was taken (days after admission)
The organism cultured
Results of 16S PCR if no positive cultures are isolated
2 ml samples for PCR will only be processed if no diagnostic cultures are recovered

Health questionnaire
We will conduct a survey amongst the survivors of the study who regained capacity, to assess their health-related quality of life using the SF-36 questionnaire. This short questionnaire will be sent to all survivors after 6 months of ICU discharge to be filled and returned by the participants.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Document the biological (biomarker) profiles of patients with severe sepsis and septic shock using genomic and proteomic analysis from samples taken on day 1,2,5 and ICU discharge
2. Identify which combinations of biomarkers can give the best predictive information of how the patient will progress in their illness using genomic and proteomic analysis from samples taken on day 1, 2, 5 and ICU discharge
3. Assess quality of life after 6 months of ICU discharge in this cohort

Key secondary outcome(s)
Assess the utility of the biomarker panel in the clinical environment as point-of-care tests on suitable devices used near the bedside

Completion date
01/07/2014

Eligibility

Key inclusion criteria
1. Aged 16 years or over
2. Diagnosis of severe sepsis. Sepsis is defined as:
2.1. A defined focus of infection: indicated by either:
2.1.1. An organism grown in blood or sterile site OR
2.1.2. An abscess or infected tissue (e.g., pneumonia, peritonitis, urinary tract, vascular line infection, soft tissue, etc)
2.2. At least two systemic inflammatory response syndrome (SIRS) criteria. The four SIRS criteria are:
2.2.1. Core temperature >38°C or <36°C (core temperature is rectal, urinary bladder, central line, or tympanic). If oral, inguinal or axillary temperatures are used, add 0.5°C to the measured value. Hypothermia <36°C must be confirmed by core temperature only. Use the most deranged value recorded in the 24 hours before ICU admission.
2.2.2. Heart rate >90 beats/minute. If patient had an atrial arrhythmia, record the ventricular rate. If patients have a known medical condition or are receiving treatment that would prevent tachycardia (for example, heart block or beta blockers), they must meet two of the remaining three SIRS criteria. Use the most deranged value recorded in the 24 hours before ICU admission.
2.2.3. Respiratory rate > 20 breaths per minute or a PaCO2 < 4.3 kPa (32 mmHg) or mechanical ventilation for an acute process. Use the most deranged respiratory rate or PaCO2 recorded in the 24 hours before ICU admission.
2.2.4. White blood cell count of >12 x 109/l or < 4 x 109/l or > 10% immature neutrophils (band forms). Use the most deranged value recorded in the 24 hours before ICU admission.
3. Severe sepsis is defined as sepsis plus at least one organ failure, except when that organ failure was already present 48 hours before the onset of sepsis.
4. Organ failure is defined as a Sequential Organ Failure Assessment (SOFA) score > 2 for the

organ in question
5. Presenting to hospital with abdominal or pulmonary sepsis of less than 72 hours duration
6. Patient already has or will require arterial cannulation as part of standard treatment

Inclusion criteria for critically ill patients without infection:
1. Patients admitted to the ICU following out-of hospital cardiac arrest
2. SIRS criteria as above
3. Organ failure criteria as above
4. Patients must not be receiving antibiotics for treatment of known or suspected infection
5. Patient already has or will require arterial cannulation as part of standard treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Age less than 16 years
2. Pregnant
3. Severe immune deficiency, for example a diagnosis of AIDS
4. Anti-rejection transplant drugs
5. Methotrexate
6. High-dose corticosteriod treatment (>10 mg prednisolone/day or equivalent)
7. Severe liver failure
8. Childs III or worse

Date of first enrolment
01/03/2013

Date of final enrolment
01/07/2014

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Institute of Infection and Immunity
Cardiff

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CF14 4XN

Sponsor information

Organisation
Cardiff University (UK)

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Research organisation

Funder Name
Technology Strategy Board (UK); Ref:101191

Alternative Name(s)
TSB

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration