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Central venous blood gas and cardiac output

Submission date	Recruitment status	[_] Prospectively registered
26/06/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/01/2012	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
28/02/2018	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Severe sepsis or septic shock occurs when your blood pressure drops to a dangerously low level after an infection. Treatment involves giving fluids through a vein and giving drugs that increase the volume of blood pumped by the heart (cardiac output). Doctors often need to know about the effect of a treatment on the cardiac output, but measuring the cardiac output requires expensive equipment. In all seriously ill patients a tube is inserted into a large vein in the chest (called a central venous catheter) to measure the blood pressure in the central veins and for giving drugs. The levels of oxygen and carbon dioxide in the central venous blood can be measured from the blood samples taken from the central venous catheter. In this study we want to find out whether changes in the levels of oxygen and carbon dioxide could be used to assess changes in cardiac output without the need for expensive equipment.

Who can participate?
Patients aged over 18 admitted to the ICU with sepsis.

What does the study involve?
All patients receive standard resuscitation treatment after being admitted to the ICU. Fluids, red blood cells and drugs are given to maintain blood pressure. A catheter is inserted into an artery to determine the cardiac output. If a patient is likely to increase cardiac output in response to fluids, fluids are given accordingly. Blood samples for blood gas analysis are drawn simultaneously from the arterial and central venous line (2 ml each). Three consecutive measurements of blood oxygen and carbon dioxide levels are performed and the average is calculated and used for further statistical analysis. Immediately after any series of blood samples cardiac output is recorded. Another set of blood samples is taken and cardiac output is measured again after the intervention to increase cardiac output is finished

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
James Cook University Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2010 to October 2011

Who is funding the study?
James Cook University Hospital and NIHR Clinical Research Network Flexibility & Sustainability Funding (UK)

Who is the main contact?
Dr Jost Mullenheim

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
10/H0907/44

Study information

Scientific Title
Can changes in central venous oxygen saturation and central venous - arterial partial pressure of carbon dioxide difference predict changes in cardiac output in septic patients?

Study objectives
We hypothesise that the trend in cerebrovascular accident (CVA): partial pressure of CO2 in blood (pCO2) difference and/or central venous oxygen saturation (ScvO2) in response to interventions targeted to increase CO can be used to assess changes in CO.

This will be investigated in 28 septic patients admitted to the intensive care unit (ICU) in which CO monitoring is deemed necessary. The results of this trial will inform the basis for further studies. Septic shock is one of the most common reasons for ICU admission. Instead of targeting a specific central venous pressure (CVP), the goal in early fluid resuscitation of patients with septic shock should be rather to optimise flow-related parameters and thus oxygen delivery in

line with the recommendation given in the latest guidelines for the treatment of sepsis. Aiming for predefined absolute values of ScvO2 is unreliable given the large limits of agreements between ScvO2 in critically ill patients and the possibility of ongoing tissue hypoxia despite normal ScvO2 values. Thus, an alternative approach of resuscitation of patients with severe sepsis or septic shock might be to titrate fluids/inotropes to achieve the individual maximum ScvO2 and/or lowest central venous-arterial pCO2 difference.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Newcastle and North Tyneside 2 Research Ethics Committee, 07/09/2010, ref: 10/H0907/44

Study design
Single centre trial

Primary study design
Observational

Secondary study design
Cohort 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
Sepsis

Interventions
1. Most patients participating in the study will be mentally incapacitated due to the influence of strong sedating drugs and underlying critical illness
2. Before the incapacitated patient is enrolled, we will seek consent from a personal consultee and a no objection form will be obtained in line with the Mental Capacity Act
3. We will also enquire about any objection through a registered lasting power of attorney for medical affairs or an advance decision precluding research. If the enrolled patient survives, he /she will be approached for retrospective consent to remain within the study
4. All patients will receive standard resuscitation treatment after being admitted to ICU as per current international guidelines for management of severe sepsis and septic shock
5. Briefly, during the initial resuscitation period (first 6 h) resuscitation goals are CVP 8-12mmHg (> 12 mmHg if mechanically ventilated), mean arterial pressure ≥65 mmHg, urine output ≥0.5 ml /kg/h]
6. Fluid boluses, red blood cells and dobutamine will be given accordingly
7. Further support consists of further fluid challenges using crystalloids or colloids to maintain CVP, if hypovolaemia is suspected or if haemodynamic improvement is observed in response to

fluid challenges
8. Vasopressors are given to maintain mean arterial pressure ≥65 mmHg (noradrenaline and additional vasopressin if no response to noradrenaline)
9. Dobutamine is started if cardiac filling pressures are elevated and CO is low
10. Advanced haemodynamic monitoring (PiCCO2®, Pulsion Medical Systems AG, Germany) is considered if despite these interventions haemodynamic stability is not achieved and lactate levels remain elevated
11. A catheter will be inserted in the brachial, axillary or femoral artery
12. SV and hence CO will be determined by transpulmonary thermodilution technique using three measurements obtained by injection of iced glucose 5% through the central line randomly throughout the respiratory cycle
13. The PiCCO2® system is a validated accurate monitor measuring SV, SVV and PPV even in rapidly changing circulatory conditions and in patients with reduced heart function
14. These parameters are continuously calculated over a 30 seconds rolling period and displayed on the monitor
15. PPV will be calculated according to the following formula (PiCCO2):
15.1. PPV (%) = (PPmax-PPmin)/(PPmax+PPmin)/2x100, where PPmax and PPmin are the maximal and minimal values of pulse pressure over a respiratory cycle, respectively
16. SVV will be calculated according to the following formula (PiCCO2):
16.1. SVV (%) = (SVmax-SVmin)/(SVmax+SVmin)/2x100, where SVmax and SVmin are the maximal and minimal values of SV over a respiratory cycle, respectively
17. PPV and SVV will be used in patients who are intubated, mechanically ventilated with a tidal volume of at least 8 ml/kg estimated ideal body weight with no spontaneous breathing activity and who are in sinus rhythm to predict whether a patient is likely to increase CO in response to a fluid challenge (= fluid responsiveness)
18. The mean threshold to differentiate responders from non-responders in septic patients is 13 % for PPV and 11 % for SVV, respectively
19. A fluid bolus (250-500ml Gelofusin) will be given accordingly unless contraindications for a fluid challenge are present (PaO_2/FiO_2 less than 13.3 kPa, hydrostatic pulmonary oedema on chest X-ray)
20. In non-ventilated patients, ventilated patients with spontaneous breathing activity, ventilation with tidal volumes < 8ml/kg or in patients with significant arrhythmias (atrial fibrillation, multiple ventricular/supraventricular extra beats) we will use passive leg raising (PLR from the 45° semi-recumbent position, to predict fluid responsiveness.
21. In these conditions Monnet and coworkers have shown that an increase in CO of at least 10% measured by the PiCCO during PLR enables a diagnosis of a positive response to fluid administration with a sensitivity of 91% and a specificity of 100%
22. This study has also shown that the PiCCO system can be reliably used to assess the haemodynamic response to PLR. Thus, PLR induced changes of CO measured with the PiCCO monitor will be used as an ideal screening manoeuvre to decide whether the patient requires ongoing fluid resuscitation in situations where PPV and SVV have been shown to be unreliable (e. g. spontaneous breathing activity, arrhythmias)
23. PLR raising will be performed every 2 h within the first 24 h after admission and every 6h thereafter
24. In any patient in whom an intervention to increase CO is planned (e.g. application of fluid bolus, start/increase of inotrope dose) blood samples for blood gas analysis will be drawn simultaneously from the arterial and central venous line (2 ml each).
25. Three consecutive measurements of $ScvO_2$, central venous and arterial pCO_2 will be performed and the average will be calculated and used for further statistical analysis
26. Immediately after any series of blood samples SV and hence CO, PPV and SVV will be recorded. Another set of lood samples will be taken and measurement of CO will again be performed after the intervention targeted to increase CO is finished (10 min after start/change

of inotrope dose, immediately after fluid bolus has been given)

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
The correlation between changes of cardiac output with changes in central venous saturation and central venous arterial partial pressure of carbon dioxide difference, respectively

Secondary outcome measures
Sensitivity and specificity of pulse pressure and stroke volume variation to predict an increase in cardiac output by at least 10%

Overall study start date
01/10/2010

Completion date
01/10/2011

Eligibility

Key inclusion criteria
1. 28 Adult patients (>18 years old)
2. Have severe sepsis or septic shock, as defined by the International Sepsis Definitions Conference (Levy MM et al, 2003)
3. Are equipped with both arterial and central line
4. In whom CO monitoring and an intervention to increase stroke volume (SV) and hence CO (e.g. fluid bolus, inotropes) is deemed necessary

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
28 patients

Key exclusion criteria
1. No consent: objection from somebody close who is willing to be consulted about the appropriateness of the patient being enrolled in the study in line with the Mental Capacity Act

objection through registered lasting power of attorney for medical affairs advance ecision precluding research retrospective withdrawal of consent
2. Pregnancy
3. Age below 18 years

Date of first enrolment
01/10/2010

Date of final enrolment
01/10/2011

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
James Cook University Hospital
Middlesbrough
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Sponsor information

Organisation
James Cook University Hospital (UK)

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Sponsor type
University/education

Website
http://www.southtees.nhs.uk/live/?a=1799

ROR

https://ror.org/02vqh3346

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
James Cook University Hospital (UK)

Funder Name
NIHR Clinical Research Network Flexibility & Sustainability Funding (UK)

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