

Central venous blood gas and cardiac output

Submission date 26/06/2011	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 24/01/2012	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 28/02/2018	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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

Contact name
Dr Jost Mullenheim

Contact details
Intensive Care Unit
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

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 \geq 65 mmHg, urine output \geq 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. $PPV (\%) = (PP_{max} - PP_{min}) / (PP_{max} + PP_{min}) / 2 \times 100$, where PP_{max} and PP_{min} 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. $SVV (\%) = (SV_{max} - SV_{min}) / (SV_{max} + SV_{min}) / 2 \times 100$, where SV_{max} and SV_{min} 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 < 8 ml/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 blood 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 decision
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

United Kingdom

TS4 3BW

Sponsor information

Organisation

James Cook University Hospital (UK)

Sponsor details

c/o Ms Julie Rowbotham

James Cook University Hospital

Marion Road

Middlesbrough

England

United Kingdom

TS4 3BW

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