ISRCTN37255045 https://doi.org/10.1186/ISRCTN37255045

Can brachial artery peak velocity variation and changes in this parameter in response to passive leg raising be used as a marker to predict fluid responsiveness in spontaneously breathing septic patients?

Submission date
13/03/2012

Recruitment status
Stopped

Registration date
08/05/2012

Overall study status
Stopped

Last Edited
15/08/2016

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
Generalised infection (sepsis) is a common reason for admission to intensive care. Intravenous fluid therapy (the infusion of liquid substances directly into a vein) is a vital part of treatment in order to treat shock and improve the blood flow generated by the heart (cardiac output). Special monitors measuring cardiac output are used to guide intravenous fluid therapy. However, this approach is restricted to intensive care as it requires expensive, invasive equipment and staff trained in using these devices. Therefore, there is a need to find other ways to guide fluid administration in patients in A&E or normal wards. It has been shown that doctors can be quickly trained to use non-invasive, hand-carried ultrasound devices. This equipment is relatively cheap, can be reused and could be made available outside of higher care wards. It allows measurement of blood flow speeds (velocities) within arm or leg arteries. We plan to investigate whether changes in blood flow velocities while breathing in and out measured in an elbow artery can be used to assess fluid status in patients with sepsis admitted to the high dependency or intensive care unit. These changes are larger if the patients blood volume is low and thus would benefit from further fluid administration. Specifically, we will investigate whether there is a specific blood flow velocity change which can predict whether the patient needs further fluid therapy, and whether measurement of the changes in blood flow velocities in response to passive leg raising (which transfers blood from leg veins to the heart) can be used for the same purpose.

Who can participate?
Adult patients who are being treated for sepsis but do not need assistance with breathing using a ventilator can take part.

What does the study involve?
Patients taking part in the study will have a number of measurements taken including blood pressure, heart rate and breathing rate. Measurements will also be taken from intravenous lines

that the patient will already have in place as part of their care. An extra measurement will be taken using an ultrasound and this will measure the speed of the blood flowing through the elbow artery. After these measurements the patient will have their legs raised to 45 degrees using the controls on their bed, and the measurements will be repeated again. They will then be repositioned back to their initial position and be given a bag of fluid through a drip, after which the measurements will be repeated once more.

What are the possible benefits and risks of participating?
Assessing the effect of raising their legs on the blood flow generated by the heart might help us to more accurately determine whether intravenous fluid should be given. Furthermore, what we learn from this study may help us to treat patients with sepsis in the future. There is no financial benefit from participation in the study. Patients taking part in the study will be closely monitored with extra readings (from the monitors they will be attached to as part of their routine care) being recorded at the same time as measuring the speed of blood flow through an artery in their elbow. Measurements of the blood speed with an ultrasound machine will not carry any additional risk.

Where is the study run from?
James Cook University Hospital - Intensive Care and High Dependency Units (UK)

When is study starting and how long is it expected to run for?
April to August 2012

Who is funding the study?
South Tees NHS Foundation Trust (UK)

Who is the main contact?
Dr Jost Mullenheim
jost.mullenheim@stees.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Jost Mullenheim

Contact details
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW
+44 (0)1642 854643
jost.mullenheim@stees.nhs.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Can brachial artery peak velocity variation and changes in this parameter in response to passive leg raising be used as a marker to predict fluid responsiveness in spontaneously breathing septic patients? a non-randomised pilot study

Study objectives
Sepsis is a common reason for escalation to higher care and carries significant morbidity and mortality (Survive Sepsis Campaign 2010 www.survivesepsis.org). Early goal directed therapy has been shown to improve patient outcome and is associated with lower mortality. Early adequate volume expansion is crucial to optimise stroke volume (SV) and hence cardiac output (CO) and oxygen delivery. Clinical examination of fluid status has been shown to be an inaccurate means of predicting patients fluid requirement. Inappropriate fluid loading can lead to tissue oedema reducing tissue oxygenation and is associated with a poorer outcome.

Traditionally used static markers of fluid responsiveness such as central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) have been shown to poorly predict the response to volume expansion in both acutely ill patients and healthy volunteers. Focus has moved towards looking at dynamic markers of fluid responsiveness using respiration induced cyclic changes in systolic pressure [systolic pressure variation (SPV)], pulse pressure [pulse pressure variation (PPV)] and stroke volume [stroke volume variation (SVV)]. These cyclic changes are more pronounced in patients with central hypovolaemia. Cut off values have been identified which can accurately predict fluid responsiveness in ventilated patients.

However measurement of these parameters is invasive and expensive as an arterial line with special haemodynamic monitors are required. These are associated with the risk of infection, haemorrhage and emboli. Invasive monitoring requires time to be set up as well as staff trained to carry out these procedures and may not be available in an accident and emergency department or a standard medical ward. Furthermore, PPV, SVV and SPV have only been shown to reliably predict fluid responsiveness if patients.
1. Are mechanically ventilated with a tidal volume of at least 8 ml/kg without spontaneous breathing activity
2. Are in sinus rhythm with no significant arrhythmias
3. Have no severe RV dysfunction

Thus, there is a need to establish new haemodynamic parameters to predict fluid responsiveness which are universally available and can be measured non-invasively in a wide variety of haemodynamically unstable patients.

It has been shown that doctors can be trained to use non-invasive, hand-carried ultrasound devices effectively after a short duration of training. This equipment is relatively cheaper, can be

reused and could be made available outside of higher care wards. Brennan et al. demonstrated that brachial artery peak velocity variation (BAPVV) correlates well with radial artery PPV using handheld ultrasound in mechanically ventilated patients.

It was investigated the use of BAPVV to predict fluid responsiveness in mechanically ventilated patients with acute circulatory failure. It was shown that BAPVV greater than 10% predicted fluid responsiveness, i.e. an increase in SV index of 15% or greater in the response to the fluid challenge with a sensitivity of 74% and specificity of 95%.

The recognized major limitation of using the dynamic parameters PPV, SVV, SPV and BAPVV is that they only provide a high sensitivity and specificity in predicting fluid responsiveness in a very limited group of patients, i.e. ventilated patients with no spontaneous breathing activity, no significant arrhythmia and no right ventricular dysfunction. However, fluid resuscitation is particularly important in the early stages of shock, where the patients might not be in a critical care facility with the arterial pressure being monitored or mechanically ventilated. Thus, finding a haemodynamic parameter predicting fluid responsiveness which can be measured non-invasively throughout the hospital in all patients would be of great importance.

Passive leg raising (PLR) is a technique used to mimic volume expansion by rapidly and reversibly transferring venous blood from the legs to the intrathoracic compartment leading to a transient increase in preload and therefore SV in preload dependent patients. The volume of this auto-fluid challenge is estimated to be between 200 and 500 ml with peak volume obtained using a combination of trunk lowering and leg raising simultaneously. PLR is a novel technique which can reliably predict fluid responsiveness in ventilated and spontaneously breathing patients who are in sinus rhythm or in the presence of arrhythmias. However, it requires measurement of SV and thus is not a routine measure in all critically ill patients. PLR induced changes in SV and aortic flow correlate well with increased CO induced by consecutive volume expansion. PLR can be used to differentiate between fluid responsive and non-responsive patients. PLR induced changes in CO were as accurate in predicting fluid responsiveness as baseline PPV and superior to SVV and SPV. The haemodynamic response to PLR predicts fluid responsiveness not only in mechanically ventilated but also in spontaneously breathing patients even in the presence of arrhythmias.

Preau et al. investigated whether PLR induced changes in SV, radial artery pulse pressure and femoral artery peak velocity variation using echo Doppler predict fluid responsiveness in spontaneously breathing patients with acute pancreatitis or severe sepsis. This study showed that changes induced by PLR in each of the three markers could be used to accurately predict fluid responsiveness in the study population. This would allow testing of fluid responsiveness in acutely ill patients outside of a high care setting using echo Doppler measurement of femoral artery peak velocity variation. Although the results of this study support the use of PLR and non-invasive Doppler measurement to predict fluid responsiveness the study population comprised few or no patients with common co-morbidities (reduced left ventricular and/or right ventricular function, peripheral vascular disease, cardiac rhythm other then sinus rhythm) and treatment with vasoactive and inotropic drugs. Thus, there is still the need to find a haemodynamic parameter predicting fluid responsiveness in routine practice. Ideally this parameter can be measured non-invasively by a wide variety of medical staff throughout the hospital in the majority of haemodynamically unstable patients.

The aim of this study is to investigate whether changes in blood flow velocities through the brachial artery in response to passive leg raising can be used to predict response to a fluid bolus in spontaneously breathing patients with sepsis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Newcastle and North Tyneside Research Ethics Committee, January 2012, ref: 11/NE/0295

Study design
Prospective non-randomised non-blinded single-centre interventional pilot study

Primary study design
Interventional

Secondary study design
Non randomised 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, spontaneously breathing patients

Interventions
1. Passive leg raising (PLR): using the control mechanism on the patients bed the trunk will be lowered to the horizontal position and legs raised between 30 and 45 degrees to the trunk. A set of measurements will be recorded within one minute of PLR. The patient will then be returned to their initial position and another set of measurements will be recorded after five minutes of repositioning.

2. Fluid infusion: after these sets of data are collected the patient will be given a 6 ml/kg lean body weight infusion of a colloid (Gelofusine®) within 30 minutes and a final set of measurements will be recorded 5 min after end of fluid infusion.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Can brachial artery peak velocity variation (BAPVV) at baseline or changes in BAPVV in response to passive leg raising predict fluid responsiveness

Secondary outcome measures

No secondary outcome measures

Overall study start date
03/04/2012

Completion date
31/08/2012

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Adults (over 18 years old)
2. Sepsis (International Sepsis Definitions Conference); confirmed presence of infectious process plus two or more:
2.1. Body temperature < 36.0 °C or > 38.0°C
2.2. Heart rate > 90 beats per minute
2.3. Respiratory rate > 20 breaths per minute / hyperventilation with a PaCO2 < 32mmHg
2.4. White blood cell count < 4,000/mm3 or > 12,000/mm3 or >10% immature neutrophils
3. Arterial line in place
4. Clinical need for fluid: one or more
5. Systolic blood pressure <90mmHg (or decrease of >50mmHg in previously hypertensive patients) or need for vasopressor drugs
6. Presence of oliguria (urine output < 0.5ml/kg/hr for at least two hours)
7. Tachycardia
8. Delayed capillary refill time (>2 seconds)
9. Presence of skin mottling

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
35

Key exclusion criteria
1. No consent
2. Objection from someone close who is willing to be consulted about the appropriateness of the patient who lacks mental capacity being enrolled in the study in line with the Mental Capacity Act

3. Under 18 years old
4. Pregnant
5. Mechanically ventilated
6. Evidence of fluid overload or pulmonary oedema
7. Allergy to Gelofusin
8. Unable to perform PLR (e.g. pelvic fracture)
9. Exclusion criteria after patients have already been enrolled in the study
9.1. Retrospective withdrawal of consent
9.2. Changes in vasopressor/inotropic requirements during the measurements
9.3. Changes in cardiac rhythm during the measurements

Date of first enrolment
03/04/2012

Date of final enrolment
31/08/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
James Cook University Hospital
Middlesbrough
United Kingdom
TS4 3BW

Sponsor information

Organisation
South Tees Hospitals (UK)

Sponsor details
c/o Ms Julie Rowbotham
James Cook University Hospital
Research and Development Department
Marton Road
Middlesbrough
England
United Kingdom
TS4 3BW
+44 (0)1642 282417
julie.rowbotham@stees.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.southtees.nhs.uk/

ROR
https://ror.org/02js17r36

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
South Tees NHS Foundation Trust (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