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VAsopressin vs Noradrenaline as Initial therapy in Septic sHock

Submission date 20/09/2012	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/09/2012	**Overall study status** Completed	
Last Edited 13/12/2018	**Condition category** Signs and Symptoms	

Plain English Summary

Background and study aims

Overwhelming infection (severe sepsis) can lead to a drop in blood pressure. This results in poor blood flow to the kidney and other vital organs. Severe infections are becoming an increasing healthcare problem. It is the 10th most common cause of death in America and it is estimated that the UK spends more than £1 billion each year treating severe infections in patients in intensive care units (ICU).

As well as antibiotics and intravenous fluids, adrenaline-type drugs are routinely used to increase blood pressure. Although usually effective at restoring blood pressure these drugs have important side effects.

Vasopressin and steroids are both naturally produced hormones that are released during times of severe illness. However, when blood pressure drops due to infection, these compensatory mechanisms often fail. Studies have shown that administering both of these drugs can help restore blood pressure and reduce the use of other adrenaline-type drugs. Recent studies found that vasopressin may be most effective if used earlier and for less severe drops in blood pressure and may have a specific role in preventing kidney failure. It may also be more effective if administered with steroids. We plan to undertake a trial to investigate if vasopressin can reduce kidney failure and the need for dialysis in patients with severe infections. We also plan to investigate if steroids cross-react with vasopressin.

Who can participate?

This study aims to recruit 412 adult patients with septic shock, being treated in 19 intensive care units (ICU) in the UK.

What does the study involve?

All patients who are clinically judged to have septic shock will be screened against the inclusion and exclusion criteria to see if they are eligible for the study. The patients will be randomised to receive either Vasopressin or Noradrenaline (Study Drug 1) by continuous infusion to stabilise their blood pressure. If the maximum limit of Study Drug 1 is reached then Study Drug 2 (hydrocortisone or placebo) will be administered. Routinely collected clinical data will be recorded on a daily basis during this time. Additional blood and urine samples will also be collected from a subset of patients on days 1, 3, 5 and 7 of the trial. Patients will be followed up at 28 days after inclusion and / or hospital discharge.

What are the possible benefits and risks of participating?
It is possible that one of the combinations of these drugs is better that then the other combinations. At the moment we do not know which combination is best. This study might help improve the treatment of people with septic shock in the future. As all the study drugs are already routinely used in the management of septic shock there is minimal extra risk from participation in this study. The doctors and nurses will watch careful for any possible side-effects and will treat them as necessary and even stop the drugs if needed. Only very small quantities of extra blood samples will be collected, usually from existing lines, but it might be necessary to collect a sample from a new needle which might result in some minor discomfort during collection and possibly a small bruise.

Where is the study run from?
The VANISH trial will run from Charing Cross Hospital, part of Imperial College London.

When is study starting and how long is it expected to run for?
It is anticipated that recruitment will start in November 2012. Participants will be recruited into the study over a period of 30 months.

Who is funding the study?
Funding has been provided by NIHR (National Institute for Health Research) - Research for Patient Benefit and Clinical Scientist award schemes.

Who is the main contact?
Mrs Neeraja Thirunavukkarasu
vanish@imperial.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mrs Neeraja Thirunavukkarasu

Contact details
ICU Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF
-
vanish@imperial.ac.uk

Additional identifiers

EudraCT/CTIS number
2011-005363-24

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
12985

Study information

Scientific Title
VAsopressin vs Noradrenaline as Initial therapy in Septic sHock: a double-blind factorial (2x2) randomised controlled trial

Acronym
VANISH

Study hypothesis
Septic shock is a condition where blood pressure reduces in response to overwhelming infections. This results in poor blood flow to the kidney and other vital organs. It is a life-threatening condition and requires emergency treatment in an intensive care unit.

Severe infections are becoming an increasing healthcare problem. It is the 10th most common cause of death in America and it is estimated that the UK spends about £700 million/year treating severe infections in patients in intensive care units.

As well as antibiotics and intravenous fluids, adrenaline-type drugs are used to increase blood pressure. Although usually effective at restoring blood pressure, these drugs have important side effects.

Vasopressin and steroids are both naturally produced hormones that are released during times of stress. However, when blood pressure drops due to infection, these compensatory mechanisms often fail. Studies have shown that administering both of these drugs can help restore blood pressure and reduce the use of other adrenaline-type drugs.

Recent studies found that vasopressin may be more effective if used earlier and for less severe drops in blood pressure.

In this study, we plan to investigate if vasopressin is more effective in reducing kidney dysfunction compared to noradrenaline when used as initial therapy in septic shock in adult patients. Also, we aim to study if there is any interaction between vasopressin and steroids in the management of septic shock.

More details can be found at http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=12985

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford A REC, First MREC approval date 30/01/2012, ref: 12/SC/0014

Study design
Double-blind factorial (2x2) randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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

Condition
Topic: Infection, Generic Health Relevance and Cross Cutting Themes; Subtopic: Infection (all Subtopics), Generic Health Relevance (all Subtopics); Disease: Infectious diseases and microbiology , Critical Care

Interventions
1. Vasopressin vs. Noradrenaline as initial vasopressor therapy and then
2. Intravenous hydrocortisone vs. placebo

Hydrocortisone, 50mg 6 hourly
Noradrenaline, Upto 12mcg/minute
Vasopressin, Upto 0.06 U/minute

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Vasopressin, noradrenaline

Primary outcome measure
Renal failure free days at day 28 post randomisation

Secondary outcome measures
1. Rates and duration of renal replacement therapy
2. Length of renal failure in survivors and non-survivors
3. 28-day, ICU and hospital mortality rates
4. Organ failure free days in the first 28 days, assessed using the serial organ failure assessment (SOFA) score
5. Organ support data assessed using the standard NHS Healthcare Resource Groups
6. Blood, plasma and urinary biomarkers of renal function and inflammation (including genetic polymorphisms)

Overall study start date
01/10/2012

Overall study end date
28/02/2015

Eligibility

Participant inclusion criteria
The target population is adult patients who require vasopressors for the management of sepsis despite fluid resuscitation.
All patients who are clinically judged to have septic shock will be screened against the specific inclusion and exclusion criteria and these criteria will be recorded in the eCRF.

Inclusion criteria will use the internationally-established consensus definitions of sepsis. In brief:
1. Fulfil 2/4 of the criteria of the systemic inflammatory response syndrome (SIRS) due to known or suspected infection vwithin the previous 24 hours. The SIRS criteria are:
1.1. Fever (>38 C) or hypothermia (< 36 C)
1.2. Tachycardia (heart rate > 90 beats per minute)
1.3. Tachypnoea (respiratory rate > 20 breaths per minute or PaCO2 < 4.3 kPa) or need for mechanical ventilation
1.4. Abnormal leukocyte count (> 12,000 cells/mm3, < 4000 cells/mm3, or > 10% immature [band] forms)
2. Hypotension despite adequate intravenous fluid resuscitation
3. Male & Female, lower age limit 16 years

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 412; UK Sample Size: 412

Participant exclusion criteria
1. Patient has received a continuous infusion of vasopressors previously during this ICU admission. Vasopressors include noradrenaline, adrenaline, vasopressin, dopamine, metaraminol, phenylephrine, and (intermittent) terlipressin
2. Regular systemic corticosteroid therapy within the previous three months (this does not include inhaled steroid therapy)
3. Known adrenal dysfunction / insufficiency
4. End-stage renal failure (i.e. requiring long term dialysis)
5. Physician and team are not committed to full active care
6. Patient is known to be pregnant
7. Patient has known acute mesenteric ischaemia
8. Patient is known to have Raynaud's phenomenon, systemic sclerosis or other vasospastic

diseases
9. Patient has been enrolled in another clinical trial of an investigational medicinal product within 30 days or is enrolled in another investigational study that might interact with the study drugs
10. Patient has a history of anaphylaxis to any study drug

Recruitment start date
01/11/2012

Recruitment end date
28/02/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
ICU Charing Cross Hospital
London
United Kingdom
W6 8RF

Sponsor information

Organisation
Imperial College London (UK)

Sponsor details
South Kensington Campus (main campus)
London
England
United Kingdom
SW7 2AZ

Sponsor type
University/education

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (UK) - Research for Patient Benefit and Clinician Scientist award schemes

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	03/07/2014		Yes	No
Results article	results	11/12/2018		Yes	No
Results article	results	15/04/2019		Yes	No
HRA research summary			28/06/2023	No	No