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Medication route in out-of-hospital cardiac arrest

Submission date
19/07/2021

Recruitment status
No longer recruiting

Registration date
16/08/2021

Overall study status
Completed

Last Edited
01/11/2024

Condition category
Circulatory System

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Each year over 30,000 people's hearts suddenly stop beating in communities around the UK (a condition known as cardiac arrest). Within seconds of this happening the person becomes unconscious. Unless the heart is restarted quickly, the brain will become permanently damaged and the person will die. Injecting drugs such as adrenaline through a vein is very effective at restarting the heart. However, for many people drugs are given too late to save them. This partly explains why less than one in ten people survive an out of hospital cardiac arrest.

Each year over 30,000 people's hearts suddenly stop beating in communities around the UK (a condition known as out-of-hospital cardiac arrest). Giving drugs, such as adrenaline, is very effective at restarting the heart. However, for many people drugs are given too late to save them. This partly explains why less than one in ten people survive an out of hospital cardiac arrest.

Current guidelines advise paramedics to inject drugs into a vein. It can take several critical minutes to put a drip in to a vein, ready to give drugs. A faster way to give drugs is to put a small needle into an arm or leg bone. This allows drugs to be given directly into the rich blood supply found in the bone marrow. Currently, none of the existing research is good enough to help paramedics decide how best to treat people with cardiac arrest.

Current guidelines advise paramedics to inject drugs in to a vein. The problem with this is it can take several critical minutes to put a drip in to a vein, ready to give drugs. A new, faster way of giving drugs is to put a small needle into an arm or leg bone. This allows drugs to be injected directly into the rich blood supply found in the bone marrow. Some research studies suggest this may be as good, if not better, than injecting drugs into the vein. Other studies suggest it may be less effective. None of the existing research is good enough to help paramedics decide how best to treat people with cardiac arrest. Both of these approaches are already currently used in NHS practice.

In this trial, we will test these two ways of giving drugs (into the vein or into the bone) to work out which is most effective at improving survival in people that have a cardiac arrest.

Who can participate?
Adults that have an out-of-hospital cardiac arrest.

What does the study involve?
Adults that have had an out-of-hospital cardiac arrest will be randomly allocated to one of two groups. In the first group, the paramedic will aim to place a needle into the bone. Once this has been successfully inserted, the paramedic will give cardiac arrest drugs, such as adrenaline, through that needle. If the paramedic cannot insert a needle in the bone after two attempts, they may decide whether to have further attempts at placing a needle in the bone or to try and place a drip in a vein. In the second group, the paramedic will aim to place a drip in a vein. Once this has been successfully inserted, the paramedic will give cardiac arrest drugs, such as adrenaline, through that drip. If the paramedic cannot insert a drip in the vein after two attempts, they may decide whether to have further attempts at placing a drip in a vein or try and place a needle in the bone. Both these treatments are already used routinely in the NHS.

Treatment in a cardiac arrest is urgent. Even very small delays may affect how likely it is that someone survives. As the patient that has had a cardiac arrest will be unconscious and there won' t be enough time to talk to a family member or friend about study involvement, we will immediately enrol individuals and defer the consent process until after the emergency situation has passed. We will speak to individuals that survive the cardiac arrest to inform them as to what has happened and seek their agreement to complete study follow-up questionnaires.

We will follow-up study participants for six-months. We will record how many patients have survived and how well they have recovered using some brief questionnaires. We will also see how long people spend on intensive care units and in hospital.

What are the possible benefits and risks of participating?
The planned treatments are already in routine use across NHS ambulance services. Placing a needle in a bone, rather than a drip in a vein, may increase how many patients survive following cardiac arrest. However, there may be some minor side-effects, such as infection, extravasation (misplacement of the needle and giving drug outside of the vein or bone), and dislodgement.

Where is the study run from?
The trial is led by the University of Warwick Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
May 2021 to September 2025

Who is funding the study?
The National Institute for Health Research (UK) Health Technology Assessment programme.

Who is the main contact?
Dr Keith Couper,

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
298182

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 49465, NIHR131105, IRAS 298182

Study information

Scientific Title
Pre-hospitAl RAndomised trial of MEDICation route in out-of-hospital cardiac arrest (PARAMEDIC3)

Acronym
PARAMEDIC-3

Study objectives
The primary objective of this trial is to evaluate the effectiveness of using the intraosseous route (small needle into an arm or leg bone) to give drugs to out of hospital cardiac arrest patients measured by survival status at 30 days.

The secondary objectives of the trial are to evaluate the effect of the intraosseous route as paramedics first method of treatment (referred to as first strategy) on the brain function, quality of life and survival of patients at other time points. It will also determine the cost-effectiveness of paramedics using the intraosseous route as their first strategy.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 12/07/2021, South Central – Oxford C Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8241; oxfordc.rec@hra.nhs.uk), ref: 21/SC/0178

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cardiac arrest

Interventions
INTERVENTIONS
Patients will be randomly allocated to receive either IO first strategy (intervention) or IV first strategy (control) through us of opaque, sequentially numbered sealed envelopes (or an equivalent system, such as peelable stickers or scratch cards). In patients randomised to the intervention group, initial vascular access attempts will be via the intraosseous (IO) route. At least two attempts at vascular access via the intraosseous route will be made. The anatomical site of IO attempts will be at the discretion of the treating ambulance clinician. In making a decision as to site selection, the ambulance clinician will be mindful of contraindications to specific sites (e.g. fracture in target bone, prosthetic limb/ joint).

Once IO vascular access has been successfully achieved, cardiac arrest drugs (including fluid) will be administered through the IO cannula. Where clinically required, more than one IO cannula may be sited.

If the treating clinician has made two attempts at vascular access via the IO route and been unsuccessful at both attempts, then further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

Where IO access fails at any point following successful insertion, further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

Following return of spontaneous circulation, the treating clinician may choose to continue to use any established IO access or to insert an intravenous cannula.

In patients randomised to the control group, initial vascular access attempts will be via the intravenous route. At least two attempts at vascular access via the intravenous route will be made. The anatomical site of IV attempts will be at the discretion of the treating paramedic. This reflects current NHS practice.

Once IV vascular access has been successfully achieved, cardiac arrest drugs (including fluid) will be administered through the IV cannula. Where clinically required, more than one IV cannula may be sited.

If the treating clinician has made two attempts at vascular access via the IV route and been unsuccessful at both attempts, then further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

Where IV access fails at any point following successful insertion, further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

CONSENT

The trial will recruit individuals that will be unconscious (having sustained a cardiac arrest) and who require time-critical treatment. On this basis, we plan to recruit individuals to the trial under a deferred consent model, in accordance with the Mental Capacity Act 2005. When patients regain capacity after being discharged from ICU, they will be approached to obtain consent. If the patient does not survive the cardiac arrest, relatives will be informed about their participants through passive methods to reduce the emotional burden during this distressing time.

DATA COLLECTION AND FOLLOW-UP

During this time information about their cardiac arrest and hospital stay will be collected from the patients hospital record by research paramedics. Information will also be obtained through data linkage sources. Long-term follow up will be conducted at 3 and 6 months following randomisation. Survival status will be obtained from NHS Digital or other electronic data sources. Quality of life questionnaires will be posted to the patient for completion at 3 and 6 months. They may be completed on the participant's behalf by someone that has a good awareness of their health state.

Follow-up for post discharge neurological outcomes and health related quality of life will be co-ordinated by ambulance services and follow an established system for contacting patients or their legal representatives ensuring effective follow up.

TIMETABLE FOR RESEARCH

The trial duration is schedule for 48 months with trial recruitment to take place over a 25 month period.

PLAN FOR INTERIM ANALYSIS/REPORT

The role of the Data Monitoring Committee and the Trial Steering committee will be to assess recruitment, the interim analyses in terms of the statistical monitoring.

SAMPLE SIZE

We will aim to recruit 15,000 patients to the trial.

PPI INVOLVEMENT

We have worked closely with patients and members of the public in designing the trial, including detailed discussions with our PPI co-applicant and presentation of the proposed trial to the Clinical Research Ambassador Group at University Hospitals Birmingham NHS Foundation Trial.

We will continue to embed meaningful patient and public involvement throughout the project, based on INVOLVE best practice guidance. We have convened a PPI group with a membership that reflects the diversity of people who are at risk of cardiac arrest. The PPI group will meet regularly throughout the trial. The group will support the development of patient and public facing information, advise on the strategy for approaching / informing patients about their

participation in the trial, and advise on how we use information collected about people. The group will support development of a communication strategy (including social media), and support the dissemination of information to the public both during and at the end of the trial.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Survival at 30 days following randomisation measured using patient records

Key secondary outcome(s))
Measured using patient records unless specified:
1. Return of spontaneous circulation and time to return of spontaneous circulation at any time follwoing randomisation
2. Survived event (sustained return of spontaneous circulation) (yes/no) at hospital handover
3. Survival at hospital discharge, 3 and 6 months following randomisation
4. Neurological function (measured by modified Rankin Scale) at hospital discharge, 3 and 6 months following randomisation
5. Health related quality of life (measured by EQ-5D-5L) at 3 and 6 months following randomisation
6. Hospital length of stay
7. Critical care length of stay

Completion date
01/09/2025

Eligibility

Key inclusion criteria
1. Out-of-hospital cardiac arrest currently receiving cardiopulmonary resuscitation
2. Requirement for vascular access to administer cardiac arrest drugs

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. Children (known or appear to be <18 years)
2. Known or apparent pregnancy
3. Already have vascular access

Date of first enrolment
12/11/2021

Date of final enrolment
01/07/2024

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
West Midlands Ambulance Service NHS Foundation Trust
Trust Headquarters
Millennium Point
Waterfront Business Park
Waterfront Way
Brierley Hill
West Midlands
United Kingdom
DY5 1LX

Study participating centre
North East Ambulance Service NHS Foundation Trust
Ambulance Headquarters
Bernicia House
Goldcrest Way
Newburn Riverside
Newcastle upon Tyne
United Kingdom
NE15 8NY

Study participating centre
London Ambulance Service NHS Trust
Headquarters: Waterloo
220 Waterloo Road

London
United Kingdom
SE1 8SD

Study participating centre
Welsh Ambulance Services NHS Trust
Unit 7
Ffordd Richard Davies
St Asaph Business Park
St. Asaph
United Kingdom
LL17 0LJ

Study participating centre
South Central Ambulance Service NHS Foundation Trust
7-8 Talisman Road
Bicester
United Kingdom
OX26 6HR

Study participating centre
North West Ambulance Service NHS Foundation Trust
Ladybridge Hall HQ
Chorley New Road
Bolton
United Kingdom
BL1 5DD

Study participating centre
East Midlands Ambulance Service NHS Trust
Trust Headquarters
Mellors Way
Nottingham Business Park
Nottingham
United Kingdom
NG8 6PY

Study participating centre
South Western Ambulance Service NHS Foundation Trust
Westcountry House
Abbey Court

Eagle Way
Sowton Industrial Estate
Exeter
United Kingdom
EX2 7HY

Study participating centre
South East Coast Ambulance Service NHS Foundation Trust
Nexus House
4 Gatwick Road
Crawley
United Kingdom
RH10 9BG

Study participating centre
East of England Ambulance Service NHS Trust Headquarters
Whiting Way
Melbourn
United Kingdom
SG8 6EN

Study participating centre
Devon Air Ambulance - Sandpiper Court
Unit 5
Sandpiper Court
Harrington Lane
Exeter
United Kingdom
EX4 8NS

Sponsor information

Organisation
University of Warwick

ROR
https://ror.org/01a77tt86

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR131105

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request
paramedic3@warwick.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		31/10/2024	01/11/2024	Yes	No
Protocol article		30/12/2023	24/01/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes