ISRCTN10480871 https://doi.org/10.1186/ISRCTN10480871

Efficacy of glyceryl trinitrate to facilitate the rewarming process during cardiopulmonary bypass

Submission date
05/08/2017

Recruitment status
No longer recruiting

Registration date
16/08/2017

Overall study status
Completed

Last Edited
13/08/2020

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Many types of cardiac (heart) surgery can only be performed with the patient being placed on a heart-lung bypass machine, otherwise known as cardiopulmonary bypass (CPB). The CPB circuit maintains a patient's cardiac output, blood pressure, oxygenation and removal of carbon dioxide, thereby keeping them alive whilst undergoing cardiac surgery. It is normal practice for a patient to be cooled whilst on the CPB machine for organ protection. Before a patient can be taken off or separated from the CPB machine their temperature has to be returned to normal, so there is a phase of rewarming before separation from the CPB machine. Glyceryl trinitrate (GTN) is a vasodilator drug that widens blood vessels. Currently it is left to the discretion of the individual anaesthetist to set the rate at which GTN is administered (infusion rate) during the rewarming phase of CPB. The infusion rate may have an impact on patient temperature and blood gas levels after the operation. There may be a slight benefit from an increased infusion rate of GTN during rewarming. The aim of this study is to find out whether an increased GTN infusion rate during the rewarming phase before separation from CPB will lead to a more thorough and complete rewarming.

Who can participate?
Patients aged over 18 undergoing cardiac surgery requiring CPB

What does the study involve?
Participants are randomly allocated to either the low or high dose GTN infusion rate during rewarming before separation from CPB. Their temperature is recorded after receiving anaesthesia, at rewarming from CPB, separation from CPB, application of surgical dressing (end of surgery) and arrival in the ICU.

What are the possible benefits and risks of participating?
Participating will help to improve care for patients undergoing cardiac surgery. GTN is already given to all patients undergoing cardiac surgery at different doses.

Where is the study run from?
Mater Misercordiae University Hospital (Ireland)

When is the study starting and how long is it expected to run for?
January 2017 to June 2019

Who is funding the study?
Mater Misercordiae University Hospital (Ireland)

Who is the main contact?
Dr Darren Mullane

Contact information

Type(s)
Scientific

Contact name
Dr Darren Mullane

Contact details
Mater Misercordiae Hospital
Eccles Street
Dublin
Ireland
7

Additional identifiers

Clinical Trials Information System (CTIS)
2017-002785-44

Study information

Scientific Title
Efficacy of glyceryl trinitrate to facilitate the rewarming process during cardiopulmonary bypass: a prospective randomised trial

Study objectives
GTN is a vasodilator drug (widens blood vessels). It has been extensively used for coronary artery vasodilatation in patients with angina, and for blood pressure reduction both on a maintenance basis and intra-operatively. GTN has been used in a medical setting for more than 100 years.

GTN administration during the rewarming phase of CPB may potentially allow a more complete rewarming, washing out peripheral cold blood containing waste products such as lactate and reducing the tendency for the patients to cool down again after the rewarming process and following separation from CPB. Currently some cardiothoracic anaesthetists at the Mater Hospital use an increased rate of GTN infusion during the rewarming phase to vasodilate blood

vessels potentially allowing a more complete washout of cold blood and waste products, facilitating the rewarming process. However, practice is heterogenous and there is no consensus approach.

One more commonly used GTN dosing regimen used at the Mater has not been examined in any robust way in the literature. An audit of Mater practice showed evidence that a GTN infusion at ~0.5mcg/kg/min caused a slower rewarming process but a more sustained normothermia post-operatively with lower lactate levels in the initial post-operative period. However, as this was merely an audit of current practice it is subject to considerable bias, given some anaesthetists use the increased GTN infusion rate during rewarming and some don't.

The trialists hypothesise that an increased GTN infusion rate during the rewarming phase prior to separation from CPB will lead to a more thorough and complete rewarming thereby reducing temperature falls and decreasing raised plasma lactate levels in the early post-operative period (whilst the patient is in ICU).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Mater Misercordiae University Hospital Institutional Review Board, 18/01/2017, ref: 1/378/1869

Study design
Prospective randomised trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cardiac surgery necessitating CPB

Interventions
All patients scheduled to undergo cardiac surgery will be reviewed as per usual by the one of the cardiothoracic anaesthesia fellows, both of whom are part of the study team.

Patients, if eligible for the study, will be given a PIL and informed about the study. Following a cool off period to allow the patient time to consider their participation in the study if the patient wishes to participate in the study they will sign a consent form. At this point baseline patient details will be recorded.

Each study subject will be randomized via a computer randomization programme to either the low or high dose GTN infusion rate during rewarming prior to separation from cardiopulmonary bypass (approximately 30-minute duration).

Standard pre-operative assessment will be performed with recording of the following baseline demographics:
1. Patient age at surgery
2. Patient gender

3. Patient height, weight, BMI and body surface area
4. Planned surgery
5. Use of vasodilator therapy pre-operatively
6. Co-morbidities including presence of peripheral vascular disease and renal impairment
7. Left ventricular ejection fraction
8. EuroScore II

Patient induction and anaesthetic care will be as standard (as per the individual anaesthetizing consultant's preference). Doses of all drugs administered during the surgical procedure will be recorded, as per standard practice. Invasive arterial pressure monitoring and central venous pressure monitoring lines will be placed as normal standard practice prior to knife to skin. All haemodynamic and temperature indices will be monitored continuously and recorded 5 minutely as standard practice.

Intra-operative:
Pre-CPB:
Standard monitoring will be initiated at induction for both groups to include:
1. Temperature monitoring:
1.1. Core (bladder)
1.2. Peripheral (nasopharyngeal)
1.3. Skin (temporal)
1.4. Urinary catheter contains bladder temperature probe.
1.5. Skin probe to be placed in temporal position.
1.6. Nasopharyngeal probe to be placed at a standardized depth: 5cm from nostril aperture.
2. Invasive blood pressure measurement, via an invasive arterial cannula
3. Arterial blood gas monitoring (standard measurements pre and post-CPB)
4. Invasive central venous pressure (CVP) monitoring
5. ECG
6. Continuous end tidal carbon dioxide and inhalational anaesthetic gas measurements
7. Continuous peripheral saturation monitoring
8. Bispectral index monitoring (depth of anaesthesia monitoring)
9. TOE monitoring if indicated by procedure

Pre-CPB conduct of anaesthesia will be standard care and at the discretion of the anaesthetizing consultant
1. Intrathecal opioid at discretion of anaesthetizing anaesthetist
2. Infusions of standard vasoactive drugs will be connected to CVP line as is standard practice and doses will be dictated by patient haemodynamic parameters as usual practice:
2.1. GTN infusion at standard concentration (30mg diluted to 50mls with 5% glucose)
2.2. Inotrope and vasopressor infusions as per preference of individual anaesthetist, at standard concentrations; to include potentially:
2.2.1. Adrenaline infusion (3mg diluted to 50mls with 5% glucose)
2.2.2. Noradrenaline infusion (3mg diluted to 50mls with 5% glucose)
2.2.3. Dobutamine infusion (200mg diluted to 50 mls with 5% glucose)
2.2.4. Other infusions again as preference of anaesthetizing anaesthetist:
2.2.4.1. Actrapid infusion at standard concentration (50 units diluted to 50mls with 0.9% sodium chloride solution)
2.2.4.2. Opioid infusion (fentanyl, remifentanil or morphine sulphate) as per preference of individual anaesthetist
3. Doses of paralysis, opioids and heparin at the discretion of anaesthetist
4. ABG monitoring as per standard procedure

Commencement of CPB:
1. Standard care with anaesthesia maintained by volatile anaesthetic into CPB circuit for both patient groups
2. Benzodiazepine and paralysis administration at the discretion of the anaesthetizing anaesthetist
3. Heparin doses as necessary to maintain ACT > 400 secs as per standard practice
4. Mean arterial pressure to be maintained at level set by anaesthetist according to patient's co-morbidities as per usual practice, usually > MAP 60-80 mmHg
4.1. Metaraminol doses as necessary to achieve MAP target
5. Study protocol does not permit the use of propofol TIVA during CPB
6. ABG monitoring as per standard procedure

Rewarming:
1. At initiation of rewarming instruction by Consultant surgeon patient will receive either:
1.1. High dose infusion: GTN infusion rate at 0.5 mcg/kg/min via CVP line
1.2. Low dose infusion: GTN infusion rate at 0.01 mcg/kg/min via CVP line
2. Once core temperature and peripheral temperatures > 36°C and patient is ready for separation from CPB circuit, GTN infusion rate will be set according to preference of the anaesthetist according to patient haemodynamics and co-morbidities
3. Time taken for completion of rewarming process (both core and peripheral temperatures > 36° C) and duration of GTN infusion (low or high rate) will be recorded
4. ABG monitoring as per standard procedure

Post-CPB:
1. On separation from CPB, rates of infusions of all vasoactive drugs will be set according to clinical need and at discretion of anaesthetist as indicated for haemodynamic control
2. ABG monitoring as per standard procedure

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Glyceryl trinitrate

Primary outcome(s)
1. Time to completion of rewarming prior to separation from CPB circuit
2. Early post-op patient peripheral – core temperature gradient
3. Time to maintenance of normothermia (core temperature > 36.5°C) for minimum of 2 hours in the initial post-op period and including skin temperature reaching a plateau
4. Plasma lactate concentrations initially post-CPB

Nasopharyngeal, skin and bladder temperature are recorded at baseline post induction of anaesthesia, rewarming from CPB, separation from CPB, application of surgical dressing (end of surgery) and arrival in ICU.

Key secondary outcome(s)
Time to extubation, measured from application of surgical dressing (end of surgery) to actual time of removal of endotracheal tube (extubation)

Completion date
14/08/2019

Eligibility

Key inclusion criteria
1. Adult patients (aged over 18)
2. Capacity to consent
3. Undergoing cardiac surgery necessitating CPB

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
82

Key exclusion criteria
1. Age < 18 years old
2. Allergy to GTN
3. Cardiac surgery necessitation deep hypothermic circulatory arrest (DHCA)
4. Cardiac surgery not involving CPB (eg. off-pump cardiopulmonary bypass grafting)
5. Lack of capacity to consent
6. Use of TIVA propofol whilst on CPB

Date of first enrolment
30/01/2017

Date of final enrolment
14/07/2019

Locations

Countries of recruitment
Ireland

Study participating centre

Mater Misercordiae University Hospital
Eccles Street
Dublin
Ireland
7

Sponsor information

Organisation
Mater Misercordiae University Hospital

ROR
https://ror.org/040hqpc16

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Mater Misercordiae University Hospital

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be coded and electronically stored in the Mater Hospital which is password protected.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	13/08/2020	Yes	No