Blood pressure and cardiac output - the influence on cerebral perfusion during cardiopulmonary bypass.

Published: 22-07-2015
Last updated: 16-04-2024

To study the influence of systemic blood flow and mean arterial pressure on cerebral blood flow and cerebral tissue oxygenation in patients undergoing on-pump cardiac surgery.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45015

Source
ToetsingOnline

Brief title
Parameters of cerebral perfusion

Condition

- Other condition

Synonym
cerebral autoregulation, oxygen regulation of the brain

Health condition

patienten aan de cardiopulmonale bypass

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Blood flow, Blood pressure, Cerebral perfusion, Near InfraRed Spectroscopy (NIRS)

Outcome measures

Primary outcome

Primary endpoints are the changes in the regional cerebral oxygen saturation

and the mean velocity of bloodflow in the middle cerebral artery.

Secondary outcome

Not applicable.

Study description

Background summary

A jeopardized cerebral blood flow (CBF) for a few minutes* results in irreversible cerebral tissue damage. Therefore, the CBF is autoregulated implying that CBF remains constant despite changes in cerebral perfusion pressure. Since the 1970s, Near Infra-Red spectroscopy (NIRS) derived frontal lobe oxygenation (rSO2) and flow velocity of the middle cerebral artery (Vmca) measured by transcranial doppler (TCD) can be used continuously and non-invasively, as a derivative for CBF. These monitoring techniques are used extensively and in the case of a decreasing rSO2, various algorithms have been proposed to optimize rSO2. One of the first steps in the algorithm is to increase blood pressure by administrating an *1*receptor mediated vasopressor like phenylephrine. However, several studies recently described that the rSO2 decreased after phenylephrine administration. It remains unknown why rSO2 decreased, but it could be a result of the *1*receptor mediated decline in cardiac output (CO). This hypothesis is supported by the finding that in patients on CardioPulmonary Bypass (CPB), i.e. with constant Cardiac Output (CO), the rSO2 only decreased with 3% after administering phenylephrine in comparison to a 10% decline in rSO2 in non-cardiac surgery. It therefore still remains unclear whether rSO2 is (more) dependent on blood pressure or on CO. Our aim is to determine whether cerebral blood flow and cerebral tissue

oxygenation is most dependent on cardiac output or on mean arterial pressure in patients undergoing cardiac surgery with the use of CPB.

Study objective

To study the influence of systemic blood flow and mean arterial pressure on cerebral blood flow and cerebral tissue oxygenation in patients undergoing on-pump cardiac surgery.

Study design

This is a randomised cross-over study.

Intervention

Interventions pre-cardiopulmonary bypass
(1) Determination of changes in cerebral tissue oxygenation and cerebral blood flow when both blood pressure and blood flow can vary.

In this intervention we will administer 50-100 *g phenylephrine to the patient before CPB is started. This intervention will take place when the patient shows hypotension (MAP <60mmHg, according to protocol22). Administering phenylephrine will increase the MAP by increasing Peripheral Vascular Resistance (PVR). Because of the increase in PVR there will be a baroreceptor-reflex-mediated decrease in CO. On-line, we will quantify the percentage decrease in systemic blood flow (i.e. CO) by using the Modelflow algoritm incorporated in a non-invasive beat-to-beat finger blood pressure monitor. This will allow us to obtain a reference for the decrease in CO to use in the next interventions. Our hypothesis is that CO will decrease because of the baroreceptor-reflex18,19.

Interventions during cardiopulmonary bypass
(2) Determination of changes in cerebral tissue oxygenation and cerebral blood flow when only systemic blood pressure is varied.

In this intervention we will induce only 1 component of the changes at intervention (1), being the increase in MAP of approximately 20 mmHg by administrating 50-100 *g phenylephrine. The CPB enables us to maintain a constant CO and thus eliminating the baroreceptor-reflex.

(3) Determination of changes in cerebral tissue oxygenation and cerebral blood flow when only systemic blood flow is varied.

With this intervention we will only create a change in CO, which enables us to eliminate the effect of blood pressure. We will modify CPB flow to achieve the CO decrease (in %) measured at intervention (1) meaning: pre-CPB after the bolus of 50-100 *g phenylephrine. In the case of unexpected increase (in %) of

CO measured at intervention (1), we will still decrease CPB flow so we will be able to analyse decrease as well as increase in CPB flow.

(4) Determination of changes in cerebral tissue oxygenation and cerebral blood flow when both the systemic blood pressure and the CO are varied as observed during intervention (1).

In this intervention we will simulate the *normal* physiological state when administering phenylephrine. We will modify CPB flow to achieve the percentage change CO as observed during intervention (1) as well as administrate 50-100 *g phenylephrine. We expect to see similar outcomes as in intervention (1).

(5) Determination of changes in cerebral tissue oxygenation and cerebral blood flow when CPB flow is raised.

In this last intervention we will create an increase in MAP without using phenylephrine but only by increasing CO. This enables us to eliminate a possible direct *1-adrenergic effect on the cerebral vasculature. MAP will be raised approximately 20 mmHg by increasing CPB flow 20%.

Study burden and risks

The burden and risks of participating in this study are negligible because all modifications will be in the physiological range. Phenylephrine used in this study will be used within its indication. There will be no time burden since all the investigations can be done just before and during cardiopulmonary bypass. There will be no follow up.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- age over 18 years
- undergoing cardiopulmonary bypass (CPB) for Coronary Artery Bypass Grafting (CABG)
- having an appropriate temporal bone window for reliable TCD monitoring
- needing pharmacological intervention because of hypotension before going on cardiopulmonary bypass.

Exclusion criteria

- requiring hypothermia during surgery
- requiring emergency surgery
- having a contraindication for phenylephrine
- having known brain pathology (e.g. Cerebral Vascular Accident (CVA) or increased intracranial pressure)
- having a history of severe carotid artery stenosis.
- having variations in hemodynamic parameters outside safe limits as described below, during the interventions
* The patient has no hypotension, defined as Mean Arterial Pressure (MAP) <60mmHg in the period before CPB
* Cardiac Output: change > 20%
* MAP: increase > 30mmHg
* Frontal lobe oxygenation (rSO2): a 20% bilateral or unilateral reduction from baseline values or an absolute decrease below 50%
* pH: <7.35 or >7.45
* Heart rate: <50 beats per minute or >80 beats per minute

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-01-2016
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO Date:	22-07-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-01-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-05-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	30-03-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT02806492
CCMO	NL52791.041.15