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The evaluation of the potential damage to vascular wall in the perioperative settings during periods of dehydration and following infusion of cristalloid solutions during general anaesthesia

Submission date
17/05/2016

Recruitment status
No longer recruiting

Registration date
10/06/2016

Overall study status
Completed

Last Edited
30/11/2020

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Patients undergoing surgery are often told not to eat or drink anything for 12 hours before the procedure, and so patients may be dehydrated when they arrive in operating room. It is standard practice to administer IV fluids (through a drip) when a person is anesthetized (put to sleep) and woken up after surgery, this technique is called volume loading (VL) and acts to control bodily processes under anesthesia. Giving too much of these fluids (hypervolemia) can lead to serious complications, including tissue edema (fluid retention), heart and lung complications and a prolonged hospital stay. Tissue edema formation at least in part is influenced by damage done to lining of blood vessels – glycocalyx, by large volumes of infused fluids. The direct mechanism of damage could be down to a substance called Brain Natriuretic Peptide (BNP), which is released from stretched heart chambers in response to hypervoleamia. The aim of this study is to analyse what happens to the fluids being infused during anesthesia, in order to find out if the standard approach used is capable of causing damage to blood vessels, and consequently tissue edema.

Who can participate?
Adults aged between 20 and 55 who are going to have a laparotomy under a general anesthetic.

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in both groups are anesthetised and then started on a type of fluid called Ringer's lactate solution (which contains similar salt concentrations as the body), at a rate of 25ml/kg in 30 minutes. For those in the first group, anaesthesia is maintained using sevoflurane (an anaesthetic that is inhaled) and for those in the second group, anaesthesia is maintained using propofol (an anaesthetic administered

through a vein). For all participants, blood and urine samples are taken just before anesthesia. Blood samples are repeated every 10 minutes and urine samples every 20 minutes starting from the beginning of fluid infusion and lasting for at least 90 minutes.

What are the possible benefits and risks of participating?
There are no direct benefits or risks involved for participants taking part in this study.

Where is the study run from?
Pauls Stradiņš Clinical University Hospital (Latvia)

When is the study starting and how long is it expected to run for?
December 2015 to December 2016

Who is funding the study?
1. Pauls Stradiņš Clinical University Hospital (Latvia)
2. Mats Mats Kleberg Foundation

Who is the main contact?
Dr Janis Nemme

Contact information

Type(s)
Scientific

Contact name
Dr Janis Nemme

Contact details
Pauls Stradiņš Clinical University Hospital
13 Pilsonu street
Riga
Latvia
LV 1002

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
R-GS2016

Study information

Scientific Title

The relationship between dehydration, fluid volume distribution and damage to the glycocalyx layer during general anaesthesia with sevoflurane and propofol

Study objectives
Primary hypothesis:
Rapid infusion of 25 ml/kg of buffered Ringer´s solution during surgery causes an increase in plasma brain natriuretic peptide (BNP)

Secondary hypotheses:
1. The fluid load causes shedding of the glycocalyx layer which possibly correlated with changes in plasma BNP
2. Rapid fluid loading, BNP increase and/or shedding own the glycocalyx layer affects the capillary leakage of albumin

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics commitee of Pauls Stradiņš Clinical University Hospital, 27/01/2016, ref: 270116 - 17L

Study design
Interventional open label randomised parallel trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

Health condition(s) or problem(s) studied
Perioperative fluid management

Interventions
Participants are randomly allocated to one of two groups using closed envelope randomisation.

Group 1: Anesthesia is gently induced with midazolam, phentanyl, propofol and atracurium without starting iv fluids. Patients are intubated, samples of blood and urine are collected again and immediately fluid load - Ringer Lactate 25 ml/kg in 30 minutes is started. The anesthesia is provided with sevoflurane, phentanyl and atracurium.

Group 2: Anesthesia is gently induced with midazolam, phentanyl, propofol and atracurium without starting iv fluids. Patients are intubated, samples of blood and urine are collected again

and immediately fluid load - Ringer Lactate 25 ml/kg in 30 minutes is started. The anesthesia is provided with propofol for 10 minutes at a rate of 10ml/kg/hour, next 10 minutes 8 ml/kg/hour and afterwards - 6-7 ml/kg/hour.

For participants in both groups, further blood samples are taken every 10 minutes till the end of infusion. After the end of infusion 4 blood samples are taken every 5 minutes and afterwards switched back to 10 minutes regimen till the end of anesthesia. Urinary samples are taken every 30 minutes starting from induction of anesthesia. Last samples are taken 2 hours after the end of anesthesia. Every time blood samples has been taken - patients blood pressure and pulse rate is documented.

Intervention Type
Drug

Drug/device/biological/vaccine name(s)
1. Sevoflurane 2. Propofol

Primary outcome measure
Brain natriuretic peptide (BNP) levels in plasma and urine after rapid fluid infusion are measured using chemiluminescent microparticle immunoassay (CMIA) at baseline (immediately before anaesthesia), immediately after anaesthesia induction, at 30 minute intervals throughout anaesthesia, and two hours after anaesthesia.

Secondary outcome measures
1. Changes in glycocalyx shedding products after rapid fluid loading are measured using ELISA at baseline (immediately before anaesthesia), immediately after anaesthesia induction, at 30 minute intervals throughout anaesthesia, and two hours after anaesthesia
2. Capillary leakage is assessed by measuring plasma albumin levels using IL Test Albumin at baseline (immediately before anaesthesia), immediately after anaesthesia induction at 10 minute intervals, every five minutes for 20 minutes after the end of fluid infusion phase, at 10 minutes intervals until the end of anesthesia and two hours after anaesthesia
3. Fluid kinetics of the infused volume of fluids are measured using Haemoglobin (Hgb) levels detected by Coulter HMX methodology at the same frequency as albumin at baseline (immediately before anaesthesia), immediately after anaesthesia induction at 10 minute intervals, every five minutes for 20 minutes after the end of fluid infusion phase, at 10 minutes intervals until the end of anesthesia and two hours after anaesthesia

Overall study start date
01/12/2015

Completion date
30/06/2018

Eligibility

Key inclusion criteria
1. Patients scheduled for elective laparotomy under general anesthesia
2. Aged between 20 and 55
3. ASA I-II

Participant type(s)

Patient

Age group
Adult

Sex
Both

Target number of participants
24

Total final enrolment
25

Key exclusion criteria
1. Urgent surgery patients
2. ASA III-IV
3. Refusal to participate
4. Pregnancy
5. Those undergoing operations under spinal or epidural anaesthesia
6. Blood loss more than 500 ml
7. Acute or chronic kidney disease

Date of first enrolment
01/02/2016

Date of final enrolment
31/12/2017

Locations

Countries of recruitment
Latvia

Study participating centre
Pauls Stradiņš Clinical University Hospital
Pilsoņu iela 13
Riga
Latvia
LV 1002

Sponsor information

Organisation
Pauls Stradiņš Clinical University Hospital

Sponsor details
13 Pilsonu street
Riga
Latvia
LV 1002
+371 67 069 601
stradini@stradini.lv

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00h1aq868

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Pauls Stradiņš Clinical University Hospital

Funder Name
Mats Kleberg Foundation

Results and Publications

Publication and dissemination plan
Planned publication in a peer reviewed journal

Intention to publish date
30/06/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	results	01/06/2016	22/06/2016	No	Yes

Results article	results	22/08/2017	30/11/2020	Yes	No
Results article		25/04/2020	30/11/2020	Yes	No