The effect of perioperative (par)enteral nutrition on amino acid profile, cardiomyocytes functioning, and cardiac perfusion and metabolism of the cardiac surgical patient.

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Our primary objective is to evaluate the effect of perioperative enteral and parenteral nutrition on amino acid profile and cardiomyocytes functioning in the cardiac surgical patient. Our secondary objective is to study the effect of the (par)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON36742

Source
ToetsingOnline

Brief title
Perioperative (par)enteral nutrition in cardiac surgery.

Condition

- Coronary artery disorders
- Cardiac therapeutic procedures

Synonym
Coronary artery disease, heart failure.

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: B.Braun,Brahms,DSM Food Specialties,Egbers Stichting,Nutricia

Intervention

Keyword: (par)enteral nutrition, amino acid profile, cardiac perfusion, cardiomyocytes function

Outcome measures

Primary outcome

The main study outcomes are concentrations of amino acids and cardiomyocytes functioning.

The amino acid profile will be studied in blood plasma and cardiac tissue (sample 1) by: determining the concentration of all amino acids, asymmetric dimethyl arginine (ADMA) and its region isomer symmetric dimethylarginine (SDMA). In cardiac tissue, also the activity of dimethylarginine dimethylaminohydrolase (DDAH, an enzyme which degrades ADMA) will be measured.

Cardiomyocytes functioning as presented by histology (sample 2): evaluation of the orientation and size of cardiomyocytes, the endocard, the interstitial, replaced and/or perivascular fibrosis, the intramyocardial vessels, glycogen stacking, hibernation of cardiomyocytes, cytosolic glycogen, iron, amyloid, CD45 (lymphocytes), CD68 (macrophages), myeloperoxidase (MPO) (neutrophil granulocytes), C3d, carboxymethyl lysine (CML), myofibril density, expanded sarcoplasmatic reticulum as marker of cellular damage, amount of mitochondria, and thickness of the basal membrane of capillaries.

We expect the concentration of several amino acids to be reduced in the cardio-surgical patient and that our nutrition will normalize these concentrations with a subsequent improvement in cardiomyocytes functioning shown by histology. Because of the arginine in the nutrition, we expect an increase in the arginine/ADMA ratio (as an indicator of nitric oxide (NO) production).

Secondary outcome

The secondary study outcomes are cardiac perfusion and cardiac fatty acid and glucose metabolism. Cardiac perfusion will be measured with 99mTc-SPECT, cardiac fatty acid metabolism with 123IBMIPP-SPECT and cardiac glucose metabolism with 18FFDG-PET.

We expect the (par)enteral nutrition to increase glucose metabolism (reflected by an increased uptake of 18FFDG by the myocardium), because the utilization of glucose as energy source by the myocardium increases under the anaerobic conditions of coronary atherosclerosis and surgery. We expect the arginine in the (par)enteral nutrition to improve the arginine/ADMA ratio and to concomitantly increase NO production and thereby improve cardiac perfusion (reflected by an increased uptake of 99mTc by the myocardium). Because the myocardium main energy source under aerobic conditions are fatty acids, we expect the increased NO production to reduce hypoxic conditions resulting in an increased fatty acid metabolism (reflected by an increased uptake of 123IBMIPP by the myocardium).

Another parameter is nutritional status. Nutritional status will be determined by measured of fat free mass by BIS. We expect that the (par)enteral nutrition to improve nutritional status reflected by an increase in fat free mass.

Other parameters are diastolic functioning by measuring diastolic pressure, cardiac function by measuring plasma levels of Troponin T, CK-MB, NT-proBNP, Copeptin (CT-proAVP), MR-proANP, MR-proADM, CT-proET-1, BrahmsX1 and BrahmsX2, switch in metabolic regulation with microRNA, and clinical parameters like ICU stay, hospital length of stay, organ failure, infections, and bleeding.

Because we expect our nutrition to normalize amino acid concentrations and to improve cardiomyocytes functioning at histological level and cardiac perfusion and metabolism, we hypothesize an improvement in blood parameters of cardiac function and a switch in metabolic regulation. The novo-cardiac parameter, BrahmsX1 and BrahmsX2, has only been studied in animal experiments and will be studied in this human study of cardio-surgical patients. In addition, because of the improvement in cardiac functioning we expect reductions in ICU and hospital stay, organ failure, infections and bleeding. As a result patients receiving our nutrition return to duties earlier.

Finally, the concentrations of ADMA and SDMA will be measured in an aortic sample because of the following. Intracellular concentrations of ADMA are more relevant than those in plasma, since generation, degradation and inhibition of NOS occur inside the endothelial cells. Therefore we are interested in the

relation of ADMA in plasma and intracellular ADMA in peripheral blood

mononuclear cells (PBMC) with intracellular ADMA in vascular tissue. The

intracellular concentrations of ADMA in PBMC should, better than concentrations

found in plasma, reflect the concentrations in the vascular wall.

Study description

Background summary

Malnutrition is very common in patients undergoing cardiac surgery as well as other types of surgery. For example, in a population of cardiac and abdominal surgical patients, respectively 9.1% and 44% was malnourished. Malnutrition can change myocardial substrate utilization which can induce adverse effects on myocardial metabolism. Interestingly, malnutrition is an underlying risk factor for the perioperative cardiac complications seen in patients undergoing non-cardiac surgery. Therefore, by optimizing nutritional status of (cardiac) surgical patients, cardiac metabolism and function might be improved. This can be done by administration of enteral or parenteral feeding.

Study objective

Our primary objective is to evaluate the effect of perioperative enteral and parenteral nutrition on amino acid profile and cardiomyocytes functioning in the cardiac surgical patient.

Our secondary objective is to study the effect of the (par)enteral nutrition on cardiac perfusion, and fatty acid and glucose metabolism.

We hypothesize there is a disturbed amino acids profile in the cardiac surgical patient and that our perioperative nutrition will normalize this profile with a subsequent improvement in cardiomyocytes functioning shown by histology, and in cardiac perfusion and metabolism which able patients to return to duties earlier.

Study design

A randomized controlled intervention study.

Intervention

Enteral group:

Four days before hospital admission, patients in the enteral group will take 250 ml of Multipower Super Charger (Shimano, Nunspeet, The Netherlands) each day consisting of amino acids (PeptoPro, DSM, Delft, The Netherlands) and carbohydrates. When admitted to the hospital, patients in the enteral group will receive a solution containing amino acids (PeptoPro, DSM, Delft, The Netherlands), carbohydrates (Fantomalt, Danone, Wageningen, The Netherlands), and vitamins and minerals (Phlexy-Vits, SHS International Ltd., Liverpool, United Kingdom) which will be prepared at the AMC. This solution will be prepared for each patient by the *speciaal keuken (afd. ADMF)* of the AMC twice a day. The enteral nutrition will be given by a post-pyloric feeding tube. It will be given three days before CABG and during CABG. The enteral nutrition will also be given the day after CABG unless the patient needs optimal (hypercaloric or hyperprotein) nutrition. An amount of 1000 ml (two times 500 ml) of the enteral feeding will be given during the day and will contain 80.5 g amino acids (12.618 g N), 95 g carbohydrates, 1.5 g fats, and 7 g vitamins and minerals which in total provide 745 kcal.

Parenteral group:
The patients in the parenteral group will receive 1250 ml of an amino acid infusion of Nutriflex Lipid peri (B.Braun, Oss, The Netherlands). The parenteral nutrition will be given three days before CABG and during CABG. The parenteral nutrition will also be given the day after CABG unless the patient needs optimal (hypercaloric or hyperprotein) nutrition. The parenteral nutrition will be given by a peripheral and/or central line (PICC). An amount of 1250 ml of Nutriflex Lipid peri (840 mOsm/L) will be given in 24 hours and contains 40 g amino acids (5.7 nitrogen/L), 80 g glucose, 50 g lipids, and electrolytes which provides 955 kcal. In addition, just before the administration of the parenteral nutrition to the patient is started, vitamins (Cernevit, Baxter, Utrecht, The Netherlands) and trace elements (Nutritrace, B.Braun, Oss, The Netherlands) will be added to the solution.

Study burden and risks

In total patients in the enteral will be asked to visit the hospital 3 times (1st: blood sampling, 99mTc-SPECT, 123IBMIPP-SPECT, 18FFDG-PET, and BIS; 2nd: blood sampling (6x), CABG, myocardial tissue (2x) and aortic tissue (1x); 3rd: blood sampling, 99mTc-SPECT, 123IBMIPP-SPECT, 18FFDG-PET, and BIS). In addition, these patients will be asked to take 250 ml of Multipower Super Charger each day four days before hospital admission. At admission, a post-pyloric tube will be placed in order to administer the enteral nutrition before (3 days), during and after (1 day) surgery.

The patients in the parenteral and control group will be asked to give to visit the hospital 2 times (1st: blood sampling (6x), 99mTc-SPECT, 123IBMIPP-SPECT, 18FFDG-PET, BIS, CABG, myocardial tissue (2x) and aortic tissue (1x); 2nd: blood sampling, 99mTc-SPECT, 123IBMIPP-SPECT, 18FFDG-PET, and BIS). At admission, a peripheral and/or central line will be placed in order to

administer in the parenteral nutrition before (3 days), during and after (1 day) surgery. The control group will receive a saline solution.

Contacts

Public
Academisch Medisch Centrum

Postbus 22700
1100 DE Amsterdam
NL
Scientific
Academisch Medisch Centrum

Postbus 22700
1100 DE Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients undergoing off-pump CABG operation
- Aged 18 till 81 years
- Having obtained his/her informed consent

Exclusion criteria

- Combined valve and coronary artery procedures
- Absent informed consent
- Aged younger than 18 and older than 80 years
- Diabetes mellitus type I
- Pregnancy
- Renal insufficiency defined as creatinine > 95 µmol/L for women and > 110 µmol/L for men
- Liver insufficiency defined as alanine aminotransferase > 34 U/l for women and > 45 U/l for men

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2010
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cernevit
Generic name:	Cernevit
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NuTRIflex Lipid peri
Generic name:	NuTRIflex Lipid peri
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Nutritrace
Generic name:	Nutritrace
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-03-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20597
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2009-017812-33-NL
CCMO	NL28231.018.09
OMON	NL-OMON20597