Glutamine metabolism in surgical patients.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26502

Source
NTR

Brief title
DIPEP HUMAN SURG

Health condition

Abdominal aneurysm, Aortic surgery, Ischemia Reperfusion Injury, Enteral nutrition, Metabolic route, Glutamine, Citrulline, Arginine, alanyl-glutamine, Kidney

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: VU University Medical Center

Intervention

Outcome measures

Primary outcome

The whole body rate of appearance of glutamine, citrulline and arginine, as well as the conversion of intravenously supplied glutamine into citrulline and arginine at the whole body level.

Furtermore, renal turnover of citrulline into arginine in patients receiving L-alanyl-L-glutamine.

Secondary outcome

The quantitative effect of aortic surgery on arginine metabolism in patients treated with or without L-alanyl-L-glutamine.

Study description

Background summary

Glutamine serves as a precursor for the de novo production of arginine through the citrulline-arginine pathway. Arginine is the precursor of nitric oxide and arginine plasma levels are important in maintaining organ blood flow. In addition to this, supplementation of glutamine could be a more physiological way to provide the human body arginine, because de novo synthesis of arginine is thought to be regulated by the kidneys. The substrate for this synthesis is citrulline. Intestinal conversion of glutamine leads to citrulline release from the gut. Thus, the intestinal-renal axis influences the effect of glutamine administration on arginine de novo synthesis.

Patients treated for abdominal aortic aneurysm often develop postsurgical renal failure, due to perioperative aorta clamping. It is plausible that those patients are inadequately converting citrulline to arginine within the kidney. As this directly consequences the arginine availability, the quantitative effects of kidney failure should be measured.

Patients develop low arginine levels after aortic surgery, however it is unknown through which metabolic route this occurs. Furthermore, the role of glutamine in this process is not unravelled yet.
In this group of patients quantification of amino acid metabolism, specifically arginine metabolism, will help adapting the enteral nutrition for those prone to kidney failure and arginine deficiency.

Objective:

The objective of this study is: To study whether glutamine given as a dipeptide administered intravenously enhances de novo arginine synthesis in surgical patients.

Furthermore, to determine the relative contribution of the kidney to this metabolic route.

Secondary objective is to determine the quantitative effect of aortic surgery on arginine metabolism in patients treated with or without L-alanyl-L-glutamine.

Outcome:

The whole body rate of appearance of glutamine, citrulline and arginine, as well as the conversion of intravenously supplied glutamine into citrulline and arginine at the whole body level.

Furthermore, renal turnover of citrulline into arginine in patients receiving L-alanyl-L-glutamine
The quantification of arginine synthesis in aortic surgery patients treated with or without L-alanyl-L-glutamine.

Design:

This is an randomized, clinical trial with 3 groups of 5 surgical patients, receiving aortic replacement surgery. Patients are randomly assigned to one of the three groups:

Group A and B: 5 patients will receive a primed continuous infusion of 0.5 g/kg/24hr L-alanyl-L-glutamine intravenously, starting 12 hours before surgery;

Group C (control group): Patients do not receive L-alanyl-L-glutamine.

Description of subjects and main criteria for inclusion:

15 Patients undergoing abdominal aortic replacement surgery will be eligible for the study. Male and female patients will be equally distributed in the different groups.

Tracers: Each group will receive stable isotopes of glutamine, citrulline, arginine, phenylalanine and tyrosine intravenously.

Group A will receive the tracers during surgery, but before aortic clamping. Group B and C wil receive the tracers after surgery.

A renal venous blood sample will be taken during surgery but before aortic clamping.

Study objective

We hypothesize that exogenous, enterally provided glutamine contributes substantially to the de novo synthesis of arginine in surgical patients.

We hypothesize that aortic replacement surgery contributes to an alteration in arginine metabolism by the kidney.

Study design

During (group A) and after (B and C) surgery, stable isotopes will be given to quantify metabolic routes.

Intervention

Group A and B: 5 patients will receive a primed continuous infusion of 0.5 g/kg/24hr L-alanyl-L-glutamine intravenously, starting 12 hours before surgery.

Group C (control group): Patients do not receive L-alanyl-L-glutamine.

Each group will receive stable isotopes of glutamine, citrulline, arginine, phenylalanine and tyrosine intravenously.

Group A will receive the tracers during surgery, but before aortic clamping. Group B and C wil receive the tracers after surgery.

A renal venous blood sample will be taken during surgery but before aortic clamping.

Contacts

Public
P.O. Box 7057
P.A.M. Leeuwen, van
Amsterdam 1007 MB
The Netherlands
+31 (0)20 4440042
Scientific
P.O. Box 7057
P.A.M. Leeuwen, van
Amsterdam 1007 MB
The Netherlands
+31 (0)20 4440042

Eligibility criteria

Inclusion criteria

1. Patients undergoing aortic replacement surgery for abdominal aneurysm;

2. Age: > 35 and < 70 years;

3. BMI < 35;

4. Having obtained his/her informed consent.

Exclusion criteria

1. Patients not fit for surgery as decided by the anesthesiology department (renal/hepatic insufficiency or heart failure);

2. Hepatitis, severe cirrhosis, urea cycle disorders/citrullinemia;

3. Kidney failure;

4. Pregnancy;

5. Corticosteroids intake in the last 4 weeks;

6. Insulin dependent diabetes mellitus;

7. Celiac disease, Crohn’s disease or other major intestinal malabsorption disorder.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2011
Enrollment:	15
Type:	Anticipated

Ethics review

Positive opinion Date:	24-05-2011
Application type:	First submission

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
NTR-new	NL2774
NTR-old	NTR2914
Other	METC VUmc : 2002-150
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
This present study is an amendment on a previous study that led to the following publications:
1. Boelens PG, Melis GC, van Leeuwen PA, Ten Have GA, Deutz NE. The route of

administration (enteral or parenteral) affects the contribution of L-glutamine to the de novo L-arginine synthesis in mice. A stable isotope study. Am J Physiol Endocrinol Metab 6 A.D. Oct;291(4):E683-90;
2. Melis GC, Boelens PG, Van dS, Jr., Popovici T, De Bandt JP, Cynober L, et al. The feeding route (enteral or parenteral) affects the plasma response of the dipeptide Ala-Gln and the amino acids glutamine, citrulline and arginine, with the administration of Ala-Gln in preoperative patients. Br J Nutr 2005 Jul;94(1):19-26;
3. Boelens PG, van Leeuwen PA, Dejong CH, Deutz NE. Intestinal renal metabolism of L-citrulline and L-arginine following enteral or parenteral infusion of L-alanyl-L-[2,15N]glutamine or L-[2,15N]glutamine in mice. Am J Physiol Gastrointest Liver Physiol 2005 Oct;289(4):G679-G685;
4. Van de Poll MCG, Ligthart-Melis GC, Boelens PG, Deutz NEP, van Leeuwen PAM, Dejong CHC. Intestinal and hepatic metabolism of glutamine and citrulline in humans. J Physiol. 2007 June 1;581(Pt 2):819-27;
5. Van de Poll MCG, Siroen MPC, van Leeuwen PAM, Soeters SB, Melis GC, Boelens PG, Deutz NEP, Dejong CHC. Interorgan amino acid exchange in man: Concequences for arginine and citrulline metabolism. Am J Clin Nutr 2007; 85:167-72;
6. Ligthart-Melis GC, van de Poll MC, Dejong CH, Boelens PG, Deutz NE, van Leeuwen PA. The route of administration (enteral or parenteral) affects the conversion of isotopically labeled L-[2-15N]glutamine into citrulline and arginine in humans. JPEN J Parenter Enteral Nutr 2007 Sep;31(5):343-8;
7. Ligthart-Melis GC, van de Poll MC, Boelens PG, Dejong CH, Deutz NE, van Leeuwen PA. Glutamine is an important precursor for de novo synthesis of arginine in humans. Am J Clin Nutr 2008 May;87(5):1282-9;
8. Ligthart-Melis GC, van de Poll MC, Vermeulen MAR, van den Tol MP, Dejong CH, Boelens PG, De Bandt JP, van Leeuwen PA. Enteral administration of alanyl-[2-15N]glutamine contributes more to the synthesis of arginine than intravenous infusion of the dipeptide in humans. Am J Clin Nutr. 2009 Jul;90(1):95-105.