The contribution of glutamine to citrulline and arginine synthesis, when alanyl-glutamine is supplied in an enteral dose of 0.5 g/kg, in critically ill patients.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON33557

Source
ToetsingOnline

Brief title
Dipep human ICU

Condition

- Other condition

Synonym
amino acid metabolism in the critically ill patient

Health condition

ernstig zieke IC patienten

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,formatie door VUmc en Medisch Centrum Alkmaar;overig door 3e geldstroom: wbso;externe sponsor (zie G2);geld gegenereerd uit internationale grant,Fresenius Kabi

Intervention

Keyword: alanyl-glutamine, enteral, glutamine, intensive care

Outcome measures

Primary outcome

The whole body rate of appearance of glutamine, citrulline and arginine, as

well as the conversion of endogenous and exogenous, enteral supplied glutamine

into citrulline and arginine at the whole body level.

Secondary outcome

First pass effect of the gut will be calculated using the difference between

the whole body rate of appearance of glutamine when the glutamine tracer is

given intravenously or enterally.

Study description

Background summary

Critically ill patients are likely to benefit from additional glutamine. Novak et al. demonstrated in their meta analysis that glutamine administration reduced morbidity and Oudemans-van Straaten showed that the magnitude of glutamine deficiency correlates with ICU mortality. In addition, low arginine and citrulline levels correlate with severity of inflammation in children. Although arginine administration can be beneficial for some groups of trauma and cancer surgery patients, its action as substrate for nitric oxide synthesis and subsequent hemodynamic instability and oxidative stress, may be responsible for doubtful results when supplied to severe critically ill

patients. Since glutamine can generate arginine by the citrulline pathway in the kidney, supplying glutamine potentially may be a more physiologic and safe way to administer arginine in the metabolically stressed ICU patient. Hence, positive effects of glutamine could be partially due to the substrate that glutamine delivers for the synthesis of arginine.
We hypothesize that exogenous, enteral provided glutamine contributes substantially to the de novo synthesis of arginine in critically ill patients.

Study objective

The objective of this clinical study is: To study whether glutamine given enterally as the dipeptide alanyl-glutamine enhances de novo arginine synthesis in critically ill patients.
Secondary objective is to determine the contribution of the splanchnic bed to this metabolic route.

Study design

Design:
This is an randomized, clinical trial with 2 groups of 10 critically ill patients
Patients are randomly assigned to one of the two groups:
Group 1 (control group): 10 patients receive enteral nutrition in the small intestine.
Group 2 (treatment group): 10 patients receive isonitrogenous enteral nutrition including 0.5 g/kg alanyl-glutamine/hr (=0.325 g/kg glutamine) in the small intestine

Intervention

Group 1 (control group): patients will receive enteral tube feeding, containing 1.5 g/kg protein/day (including 0,15 g/kg/day glutamine) for at least 5 days.
Group 2 (treatment group): patients will receive enteral tube feeding for 5 days + 0.5 g/24hr alanyl-glutamine containing 1.5 g/kg protein (including 0.15 g/kg/day glutamine).
Both groups: the tracer protocol will be performed on the 4th and 5th day after (after at least 3 days of enteral feeding). In randomized order the glutamine tracer will be given enterally or parenterally. The tracer protocol will be started between 8:00 and 10:00 in the morning and last 2.5 hours.

Study burden and risks

Potential risk is estimated at a minimum, morover potential benefits of glutamine administration are documented

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: > 18 and < 80 years
*BMI > 18,5 and < 35
*Ability to tolerate enteral nutrition, provided by postpyloric tube, meeting full protein/energy requirements based on indirect calorimetric measurements
*Expected ICU or medium care stay of a minimum of 5 days
*Any ICU patient who is considered *stable*:
* Hemodynamics: no new vasoactive medication during 24 hrs preceding inclusion, maximum dose of vasoactive medication < 5 mg/kg/min
* Respiration: PaO2/FiO2 ratio > 200, PEEP < 15 cm H2O, when on respiration
*Having obtained his/her or his/her legal representative*s informed consent

Exclusion criteria

* Admission after elective surgery
* Pregnancy
* Liver failure, defined by bilirubin levels > 100
* Kidney failure, represented by increase in serum creatinine levels to > 100 umol/l, in the absence of primary underlying renal disease, or oliguria, defined as urine output < 20 ml/hour in the previous 6 weeks
* Urea cycle defects
* Chronic corticosteroids use (> 7. mg/ day > 3 weeks)
* Bowel malabsorption possibly interfering with intestinal absorptive function, e.g. celiac disease, crohn*s disease, presence of fistulas, major intestinal malabsorption disorder, or short bowel syndrome
* Parenteral feeding
* Use of medium chain triglycerides or glutamine/citrulline supplements

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-10-2010
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	02-09-2009
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
CCMO	NL25838.029.09