Evaluation of the citrulline generation test (CGT) using intravenous administration of glutamine-alanine in ICU patients with multiple organ dysfunction.

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Primary aimTo apply the CGT (intravenously and arterial sampling) in patient with multiple organ failure for the assessment of enterocyte function as a measure for intestinal (small bowel) barrier function.Secondary aimsTo compare the CGT with other…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON33173

Source
ToetsingOnline

Brief title
Small bowel function in MODS

Condition

- Other condition
- Bacterial infectious disorders
- Respiratory tract infections

Synonym
multiple organ dysfunction syndrome, multiple organ failure

Health condition

multiorgaan falen na sepsis, trauma, pancreatitis, shock, etc

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,subsidie divisie IV nutriciagelden

Intervention

Keyword: citrulline, enterocyte function, multiple organ dysfunction syndrome, small bowel function

Outcome measures

Primary outcome

results of CGT testing: baseline citrulline levels, citrulline generation (AUC)

after stimulation with intravenous glutamine

sugar absorption testing to define intestinal permeability

assessment of intestinal absorption using bombcalorimetry

Secondary outcome

comparison of primary parameters with nutritional indices and prognostic

outcome parameters

Study description

Background summary

Citrulline, a non-protein amino acid (not incorporated into proteins), is produced by the small intestine from its precursor glutamine and subsequently

released into the systemic circulation unaffected by the liver. Citrulline is subsequently converted into arginine by the kidney. Since the small bowel is by far the main source of circulating citrulline, this amino acid is thought to be an attractive marker of enterocyte function.
Fasting plasma citrulline concentrations, however, cannot be used in this context. Therefore, the so-called *citrulline generation test* (CGT) was developed in which we assessed the enterocyte capacity to convert orally administered glutamine into citrulline. We observed a significant rise (about 40% on average) in plasma citrulline concentrations following a standardized oral bolus of alanine-glutamine (Dipeptiven) in all healthy subjects (n=20). In contrast, patients with known enterocyte dysfunction displayed a more attenuated or even absent rise in plasma citrulline concentrations. Therefore, this new test appeared to hold promise for better diagnostic accuracy for detection of enterocyte dysfunction compared to fasting citrulline concentrations. In addition, the CGT was able to differentiate patients with enterocyte damage due to coeliac disease, short bowel syndrome and radiation enteritis from healthy subjects.

Significant malabsorption has been shown to frequently occur in critically ill patients in the ICU, possibly related to diminished intestinal blood flow. At present, we have no ideal tools to assess malabsorption or enterocyte function in these critically ill patients. Faecal fat loss can be examined, as well as faecal energy loss, however, clinical data concerning these methods are limited. Sugar absorption tests are often used to detect mucosal hyperpermeability, but difficult to interpret and hampered by disturbed renal function or intestinal transit time. Therefore, we propose that the CGT may well be a useful tool in identifying ICU patients at risk for malabsorption by applying a more functional assessment of enterocyte function.
Recently, we performed a study in order to derive discriminatory/reference CGT values in the ICU setting, and the primary aim of this study was to assess CGT values in *stable* ICU patients who tolerated enteral nutrition fully meeting their protein-energy requirements. Secondly, we determined whether there are any differences in CGT curves between oral and intravenous administration of glutamine. The latter administration route might be more feasible in ICU patients, by eliminating the potential effects of decreased or increased gastro-intestinal transit time, as changes in transit time theoretically might induce erroneous CGT outcomes following enteral administration of glutamine. In addition, we put the hypothesis forward that the CGT curve obtained following oral glutamine merely reflects function of the (proximal) small bowel. In contrast, intravenous glutamine administration can be utilized by the complete small intestine by arterial extraction. This might, in theory, produce CGT curves reflecting enterocyte function (capacity) of the entire small intestine rather than just the proximal part. A tertiary aim was to determine differences in plasma citrulline concentrations when sampled venous and arterial, respectively. In this previous study we found that intravenous glutamine administration resulted in the highest citrulline responds and least variation and that arterial citrulline sampling induced higher citrulline values compared

to venous sampling.

In the current study (proposal) we aim to extent these CGT discriminatory values patients with multiple organ failure to determine whether this group suffers from enterocyte dysfunction. As stated earlier, the CGT closely reflects the ability of the enterocyte to convert glutamine into citrulline, thus representing the enterocyte function capacity
In addition, such assessment may be important with regard to stratifying nutritional support and monitoring intestinal barrier function

Study objective

Primary aim
To apply the CGT (intravenously and arterial sampling) in patient with multiple organ failure for the assessment of enterocyte function as a measure for intestinal (small bowel) barrier function.

Secondary aims
To compare the CGT with other methods assessing (mal)absorption and small bowel function such as bomb calorimetry and sugar absorption tests.
To correlate CGT values with diagnostic categories, severity of illness, severity of organ failure, and nutritional indices.

Study design

prospective observational study

Study burden and risks

The CGT is already incorporated in our unit for diagnostics in patients eg. with short bowel syndrome. There are no risks involved, it is a routine procedure with blood taken from a arterial line.

The sugar absorption test also is a routine test, with the administration of a glucose mixture through a nasogastric or duodenal tube and the collection of urine. No risks are involved.

Bomcalorimetry involves the 72 hr collection of faeces through a feaces-collector, which is a routine procedure.

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 between 18-80 years;informed consent;The presence of multiple organ dysfunction syndrome (MODS), defined as more than 2 failing organs, irrespective of the aetiology (page 5, protocol)

Exclusion criteria

*Documented causes of small bowel malabsorption possibly interfering with intestinal absorptive function, e.g. coeliac disease, Crohn*s disease of the small bowel, exocrine pancreatic insufficiency, radiation enteritis or short bowel syndrome.
*Small intestinal resections and/or extensive colonic resection (> 2/3).
*Liver cirrhosis Child-Pugh B or C, acute liver failure or renal failure requiring artificial support (e.g. CVVH).
*Urea cycle defects/citrullinaemia.
Pregnancy (no long-term data are available on the effects of Dipeptiven during pregnancy or lactation).
*Use of (par)enteral medium chain triglycerides (MCT) or glutamine/citrulline supplements.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2009
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	24-03-2009
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	NL26364.029.09