Arginine supplementation in severe sepsis: effects on metabolism and microcirculation.

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NO synthesis is compromised during sepsis through lack of L-arginine and may thereby contribute to impaired microcirculation and organ dysfunction. Supplementation of L-arginine in septic patients can replete L-arginine deficiency and will improve...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21371

Bron
Nationaal Trial Register

Verkorte titel
Arginine-sepsis study.

Aandoening

Severe sepsis or septic shock ICU patients.

Ondersteuning

Primaire sponsor: Novartis Consumer Health - R&D Nutrition.
Overige ondersteuning: N/A

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Microcirculation.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:

Sepsis is a severe clinical problem with a high mortality rate, which is caused by a severe inflammatory response to an infection. Nitric oxide (NO), which is produced by the body from the amino acid L-arginine, has an important role in the pathophysiology of the disease. NO has an important role as a vasodilator and therefore is important for vascular perfusion. In a previous study we observed that plasma arginine levels were lowered in sepsis. Moreover, L-arginine supplementation approved to be beneficial in a pig model of sepsis. This has led us to the hypothesis that sepsis is an arginine deficiency state (Luiking, CCM 2004;32:2135-45) and that patients could benefit from L-arginine administration in order to enhance NO production and improve organ perfusion and function.
Aim: The aim of our present study is to study the effects of L-arginine administration on NO production and microcirculation in a placebo controlled, double blind randomized study design.
This information adds to our understanding of the mechanism by which L-arginine supplementation may benefit septic patients. This can be a base for larger trials on arginine supplementation in the future.

Doel van het onderzoek

NO synthesis is compromised during sepsis through lack of L-arginine and may thereby contribute to impaired microcirculation and organ dysfunction. Supplementation of L-arginine in septic patients can replete L-arginine deficiency and will improve microcirculation, vascular permeability, and organ function.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

1. 3-days intravenous L-arginine infusion;

2. 3-days intravenous L-alalanine (placebo) infusion.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Written informed consent from close relative;

2. Age > 18 years;

3. Patient meets the general criteria for severe sepsis or septic shock (International published sepsis definitions), diagnosed less than 48 h prior to study inclusion;

4. Patient must be relatively hemodynamically stable, defined as stable blood pressure (variation in mean arterial pressure <15 mm Hg) during 2 h without necessity of increasing the vasopressor dose, inotropic support or rate of fluid administration;

5. Systemic arterial catheter in place with continuous pressure monitoring;

6. Patients in whom the clinician is prepared to provide full life support during the duration of the study.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Shock due to any cause other than sepsis (e.g. drug reaction or drug overdose, pulmonary embolus, burn injury, severe blood loss etc.);

2. Prolonged or high dose corticosteroid use;

3. Liver cirrhosis;

4. Chronic pancreatitis;

5. Insulin-dependent diabetes mellitus;

6. Metastases, haematological, malignancies or chemotherapy;

7. Patients on dialysis (CVVH or other);

8. Pre-existent urea cycle disorders or renal failure.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	15-11-2004
Aantal proefpersonen:	16
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	23-09-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL383
NTR-old	NTR423
Ander register	: MEC 04-136
ISRCTN	ISRCTN56258935

Resultaten

Samenvatting resultaten

1. Luiking, Y. C., Poeze, M., Dejong, C. H., Ramsay, G. & Deutz, N. E. (2004) Sepsis: an arginine deficiency state? Crit Care Med 32: 2135-2145.

2. Bruins, M. J., Soeters, P. B., Lamers, W. H. & Deutz, N. E. (2002) L-arginine supplementation in pigs decreases liver protein turnover and increases hindquarter protein turnover both during and after endotoxemia. Am J Clin Nutr 75: 1031-1044.

3. Bruins, M. J., Luiking, Y. C., Soeters, P. B., Lamers, W. H., Akkermans, L. M. & Deutz, N. E. (2004) Effects of long-term intravenous and intragastric L-arginine intervention on jejunal motility and visceral nitric oxide production in the hyperdynamic compensated endotoxaemic

pig. Neurogastroenterol Motil 16: 819-828.