Pharmacokinetics of two high dose regimes of intravenous vitamin C in critically ill patients

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To determine the pharmacokinetics of two high dose regimens of intravenous vitamin C in critically ill patients, in particular the attained plasma concentration and the fraction retained in the body and excreted in urine.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON42302

Source
ToetsingOnline

Brief title
Pharmacokinetics of intravenous vitamin C in critically ill patient

Condition

- Other condition

Synonym
sepsis, trauma

Health condition

sepsis of SIRS (systemische inflammatie) met orgaanfalen

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Onderzoeksreserve van de afdeling Apotheek.

Intervention

Keyword: Antioxidants, Critically ill, Pharmacokinetics, Vitamin C

Outcome measures

Primary outcome

Primary endpoints are plasma concentrations and pharmacokinetic parameters clearance (Cl), volume of distribution (Vd) and elilmination half life (T*), the fraction of retained vitamin C in the body and the fraction/amount of vitamin C excreted in urine.

Secondary outcome

Secondary endpoints are effect and safety parameters: oxidative damage (F2 isoprostanes), leukocyte reactive oxygen species (ROS) activity in blood and the development of high anion-gap acidosis. Explorative endpoints are clinical and biochemical markers of circulation, organ function and injury: sublingual microcirculation, renal resistive index, changes in noradrenalin dose, serum creatinine and SOFA score, and the bioimpedance markers resistance, reactance and phase angle.

Study description

Background summary

Critically ill patients with trauma or sepsis exhibit a high degree of vitamin C deficiency at ICU admission and vitamin C plasma concentrations decrease even

more during the first three days of admission. Vitamin C is a natural anti-oxidant and crucial for endothelial and organ protection

Study objective

To determine the pharmacokinetics of two high dose regimens of intravenous vitamin C in critically ill patients, in particular the attained plasma concentration and the fraction retained in the body and excreted in urine.

Study design

Prospective randomized controlled pharmacokinetic intervention study

Intervention

Patients will receive a daily dose of either 2 or 10 gram vitamin C by intermittent dosing (half of the daily dose b.i.d.) or by continuous infusion for two days.

Study burden and risks

Three ml blood will be sampled at baseline, T=1, 2, 4, 8 and 12 hours (trough level for intermittent dosing) after the first vitamin C dose or start of vitamin C infusion and a urine sample from the first 12 hours urine collection (T=0 to T=12 hours) will be taken for determination of vitamin C concentration. Vitamin C samples (trough samples for intermittent dosing) will be taken at T=24 and T=36 hours. After the last vitamin C dose or end of the infusion, blood samples will be taken at T=48, T=72 and T=96 hours. Samples for secondary and explorative endpoints will be taken at baseline and thereafter different times per parameter. A total of 48 ml blood will be taken during a period of five days from an arterial line which is routinely present for monitoring. The patient will not notice the sampling. The sampling will not impose any risk to the patient. In addition, sublingual measurement of the microcirculation, renal echography and bioimpedance measurement will be performed.

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

>18 years
Sepsis or SIRS (systemic inflammatory response syndrome), after major surgery or trauma
Non-neurological sequential organ failure score (SOFA) >6
Expected length of ICU stay >96 hours
Informed consent initially the legal representative and later by the patient

Exclusion criteria

Admission after out of hospital cardiac arrest
Prior use of supplemental vitamin C in the week before
Major bleeding
Pre-existent renal insufficiency defined as an eGFR < 30 ml/min/1.73 m2 (stadium 4-5)
Expected need for renal replacement therapy within 48 hours
Known glucose 6-phosphate dehydrogenase deficiency
History of urolithiasis or oxalate nephropathy
Previous use of prolonged high dose vitamin C supplements
Hemochromatosis

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-03-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Vitamin C
Generic name:	Ascorbic acid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-09-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2015
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-003680-38-NL
CCMO	NL50578.029.15