N-Acetylcysteine In The Treatment of Sickle Cell Disease

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We hypothesize that treatment of sickle cell patients with NAC results in reduced red cell PS exposure, reduced endothelial activation, increased NO availability, reduced coagulation activation and reduced inflammation detectable with specific...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23090

Bron
NTR

Verkorte titel
NAC in SCD

Aandoening

sickle cell disease (anemia), hypoxia-reperfusion injury, endothelial damage, oxidative stress, NO-availability, inflammation, sikkelcelziekte, chronische ontsteking, endotheelschade.

Ondersteuning

Primaire sponsor: This project will be carried out by the CURAMA programme, which is a collaborative effort between the Department of Vascular Medicine, Academic Medical Center (Amsterdam, the Netherlands), the Department of Internal Medicine Slotervaart Hospital (Amsterdam, the Netherlands), the Department of Internal Medicine, Sint Elisabeth Hospital (Curaçao, Netherlands Antilles), Red Cross Bloodbank Foundation Curaçao (Curaçao, Netherlands Antilles), the Laboratory of Clinical Thrombosis and Hemostasis in the Department of Internal Medicine, Academic Hospital Maatsricht (Maastricht, the Netherlands), the Department of Clinical Chemistry (Groningen, the Netherlands) and the department of Hematology, Erasmus Medical Center (Rotterdam, the Netherlands). CURAMA is embedded in the Antillean Institute of Health Research.
Overige ondersteuning: fund = initiator = sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Primary end-points are the effects of NAC on the laboratory markers (hemoglobin, red blood cell counts, reticulocyte counts, leukocyte counts and differentiation, platelet counts, erythrocyte sedimentation rate, a blood smear will be analyzed microscopically for the number of ISC per field, as well as the number of Heinz bodies, intra-erythrocytic GSH and GSSG levels, NO availability, SRBC phosphatidylserine (PS) exposure, annexin V, creatinine, BUN, electrolytes, transaminase levels, albumin levels, LDH, indirect bilirubin levels, free hemoglobin levels, high sensitive CRP, sVCAM-1, ET-1, IL-8, pro-thrombin fragments (F1.2), D-dimer levels, protein S (free and total) and C activity, vWF-Ag activity).

Toelichting onderzoek

Achtergrond van het onderzoek

The pathophysiology of sickle cell vasoocclusion is of a complex nature. It is now clear that, next to erythrocyte rigidity, the pathophysiology of sickle cell vasoocclusion involves cytokines, adhesion molecules, thrombus formation, platelet-, leukocyte- and endothelial activation, reactive oxygen species (ROS). Thus, it seems that in vivo, a complex interplay between many biological factors determine the extent to which vasoocclusion occurs in a given patient.
Gluthation (GSH), an amino-thiol (a thiol is a molecule with a SH group) is the most abundant antioxidant in our body and is a crucial defense against free radicals. Our body is equipped with a vast array of antioxidant substances for protection against oxidative stressors in health (varying from sun-light exposure to tobacco smoking) and disease (atherosclerosis, sepsis). NAC is highly permeable to cell membranes and within the cytoplasm it is converted to L-cysteine, which is a precursor to GSH. It is well known as a mucolytic agent and for treatment of acetaminophen induced liver toxicity. NAC has been investigated for treatment of many disease states, such as cardiovascular disease, human immunodeficiency virus infections, sepsis and acute respiratory distress syndrome. NAC is an important antioxidant with pleiotropic effects on inflammation and vasomotor function. Reactive oxygen species (ROS) may play a central role in the pathophysiology of SCD related vascular occlusion and organ damage, and NAC administration to patients with SCD may be of benefit via several mechanisms as detailed below.
Objectives:
To determine whether NAC therapy results in decreased red cell PS exposure, endothelial activation, inflammation, and reduction in clotting activation in the steady state.

Doel van het onderzoek

We hypothesize that treatment of sickle cell patients with NAC results in reduced red cell PS exposure, reduced endothelial activation, increased NO availability, reduced coagulation activation and reduced inflammation detectable with specific laboratory testing, as well as a reduction of ISC's and Heinz Body formation

Onderzoeksproduct en/of interventie

N-acetylcysteine 1200 mg or 2400 mg a day.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. High performance liquid chromatography confirmed diagnosis of HbSS, HbSC or HbSâ genotype .
2. Aged 18-65 years
3. Written informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Bloodtransfusion in the preceding four months.
2. Pregnancy or the desire to get pregnant in the following 7 months.
3. Concommitant use of hydroxyurea, vitamin K antagonists or other oral anticoagulants, or contraindications for NAC.
4. Impaired renal function of more than 60% (as assessed by the Kockroft-Gauld equation)
5. Known gatsric or duodenal ulcer
6. Concomittant use of anti-hypertensives, sildefanil or nitrates.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-10-2007
Aantal proefpersonen:	10
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	03-07-2007
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	NL985
NTR-old	NTR1013
Ander register	:
ISRCTN	ISRCTN28828586

Resultaten

Samenvatting resultaten

(1) Duits AJ, Schnog JB, Lard LR, Saleh AW, Rojer RA. Elevated IL-8 levels during sickle cell crisis. Eur J Haematol 1998; 61(5):302-305.
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