Ascorbic Acid Treatment in CMT1A Trial.

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Ascorbic acid has shown to have a favorable influence on myelination in in vitro studies and in a mouse model for CMT1A. We will study the efficacy and safety of ascorbic acid treatment in young patients with CMT1A.

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

Samenvatting

ID

NL-OMON26033

Bron
Nationaal Trial Register

Verkorte titel
AATIC

Aandoening

Charcot-Marie-Tooth Disease Type 1A (CMT1A) or
Hereditary Motor and Sensory Neuropathies (HMSN Ia)

Ondersteuning

Primaire sponsor: Department of Neurology
Academic Medical Center, University of Amsterdam
P.O.Box 22660
Amsterdam, Netherlands
Overige ondersteuning: -

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Change in motor nerve conduction velocity of the median nerve after 1 year.

Toelichting onderzoek

Achtergrond van het onderzoek

Charcot-Marie-Tooth type 1A (CMT1A), or hereditary motor and sensory neuropathy type Ia (HMSN Ia), is an autosomal dominant disease, most often caused by a 1.5 Mb duplication of chromosome 17, giving rise to three copies of the peripheral myelin protein 22 gene (PMP22). Mutations in this gene rarely cause CMT1A. It is a primarily demyelinating neuropathy, as has been shown in nerve conduction studies and in histopathological investigations. The conduction velocities of peripheral nerves are already slowed at the age of five years. Longitudinal data show that these conduction velocities do not change during life, indicating that the degree of demyelination is rather constant during life.
CMT1A is characterized clinically by distal muscle weakness and wasting, legs more than arms, impaired distal sensation, and reduced or absent reflexes. Moreover, foot and hand deformities are often encountered. In childhood, disease progression has been shown. In adults, there are indications for disease progression, but properly conducted longitudinal studies are awaited. Cross-sectional studies show that disease severity in adults is variable: a group of CMT1A patients is asymptomatic (5-10%), whereas other patients are wheelchair dependent (5-10%), still most have the classical CMT phenotype. Therapy is symptomatic and aims at maintaining functional possibilities and learning compensation mechanisms. There is no medication available that stabilizes or improves the clinical signs and symptoms.

Ascorbic acid is needed in in vitro studies for proper myelination of axons (in cultures containing serum). Recently, in a mouse model for CMT1A it has been shown that ascorbic acid improves the CMT1A phenotype. Mice (2-4 months old) treated with ascorbic acid once a week during three months showed an increase in the percentage of myelinating nerve fibers and showed better results in locomotor tests.
In this phase 2 study we will study the efficacy and safety of ascorbic acid in young patients with CMT1A. We will investigate whether ascorbic acid induces remyelination by measuring the nerve conduction of a peripheral nerve during a one year study period. CMT1A patients aged 12 years or older may cooperate sufficiently in nerve conduction studies. We include young patients, as clinical signs and symptoms especially develop relatively early in life. These signs and symptoms are due to axonal dysfunction, secondary to the demyelination. This is why we will investigate additionally whether there is an effect of ascorbic acid treatment on axonal function, strength and disabilities.

Doel van het onderzoek

Ascorbic acid has shown to have a favorable influence on myelination in in vitro studies and in a mouse model for CMT1A. We will study the efficacy and safety of ascorbic acid treatment in young patients with CMT1A.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

Ascorbic acid 1000 mg (4 capsules of 250 mg) twice daily during one year or placebo in 4 capsules twice daily during one year.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. DNA-proven CMT1A patients;

2. Age 12-25 years;

3. CMT 1A patients with symptomatology defined as muscle weakness in at least foot dorsiflexion.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Due to possible influence on severity of the neuropathy:

a. Known other disease that may cause a neuropathy, that may decrease mobility, or that may lead to severe disability or death in a short time;

b. Medication that may cause a neuropathy;

c. Chronic alcohol abuse;

2. Due to study medication (ascorbic acid):

a. Regular use of vitamin C;

b. Clinical or echographic signs of nephrolithiasis;

c. Reduced glomerular filtration rate;

d. Iron overload;

e. No regular dental control at the dentist;

f. Pregnancy or active pregnancy wish for women;

3. Due to study design and primary outcome:

a. Not signing the informed consent;

b. Psychiatric co-morbidity which may influence compliance;

c. Not being comfortable during nerve conduction studies of the median nerve;

d. A too small CMAP amplitude of the abductor pollicis brevis muscle for a proper determination of the nerve conduction velocity of the median nerve.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-11-2005
Aantal proefpersonen:	12
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	24-10-2005
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	NL394
NTR-old	NTR434
Ander register	: N/A
ISRCTN	ISRCTN56968278

Resultaten

Samenvatting resultaten

Passage E, Norreel JC, Noack-Fraissignes P, Sanguedolce V, Pizant J, Thirion X, Robaglia-Schlupp A, Pellissier JF, Fontes M. Ascorbic acid treatment corrects the phenotype of a mouse model of Charcot-Marie-Tooth disease. Nat Med. 2004 Apr;10(4):396-401. Epub 2004 Mar 21. : 15034573;

Verhamme C, van Schaik IN, Koelman JH, de Haan RJ, Vermeulen M, de Visser M. Clinical disease severity and axonal dysfunction in hereditary motor and sensory neuropathy Ia. J Neurol. 2004 Dec;251(12):1491-7. : 15645349.