The influence of Vitamin B12 deficiency on the expression of Leber Hereditary Optic Neuropathy (LHON)

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To investigate if a vitamin B12 deficiency has a higher prevalence in LHON patients, during the acute phase of visual loss, then in a normal population.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vision disorders
Study type	Observational invasive

Summary

ID

NL-OMON36113

Source
ToetsingOnline

Brief title
LHON and vitamin B12 deficiency

Condition

- Vision disorders

Synonym
genetic disease of the optic nerve, Leber Hereditary Optic

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: LHON, Vitamin B12 deficiency

Outcome measures

Primary outcome

Prevalence of a vitamin B12 deficiency in the LHON and control population.

Secondary outcome

Cause of vitamin B12 deficiency in the LHON patients

Study description

Background summary

Leber Hereditary Optic Neuropathy (LHON) is an optic neuropathy, leading to visual loss at a relative young age. In most patients a mutation in mitochondrial DNA can be demonstrated. This mutation can lead eventually to a apoptosis of retinal ganglion cells and their axons. These axons form the optic nerve. Not all LHON carrirers develop an optic neuropathy. It is known that the expression of LHON can be influenced by external factors. Smoking is mainly accepted as a precipitating factor.
A vitamin B12 deficiency can also lead to an optic neuropathy. The clinical signs of this optic neuropathy resembles that of LHON. Vitamin B12 is involved in the regulation of biochemical processes of mitochondria (methionin synthetase). In the literature, a vitamine B12 deficiency is not reported as a risk factor for the development of an optic neuropathy in patients with a positive LHON mutation. However, both the LHON mutation as the vitamine B12 deficiency have their origin in the mitochondrial metabolism. There are some case reports suggesting a link between these two factors.
Recent recommendations report that a vitamin B12 deficiency can be overlooked by a simple serum measurements of only vitamin B12. Measurement of methylmalonic acid (MMA) and homocystein (HC) give a much higher sensitivity. Both are metabolites in pathways regulated by vitamin B12 and become elevated in a deficiency.
In this way, in a two years period, we recently diagnosed a vitamin B12 deficiency in two LHON patients. These were the only two new LHON diagnosed at our department during that period. Also, a few years ago we have diagnosed vitamin B12 deficiencies in three more LHON patients. These three patients were published as case reports. These data do suggest that a vitamin B12 deficiency

can precipitate an optic neuropathy in LHON carriers.

Study objective

To investigate if a vitamin B12 deficiency has a higher prevalence in LHON patients, during the acute phase of visual loss, then in a normal population.

Study design

Prospective case-control

Intervention:
-bloodmeasurement of vitamin B12, MMA, HC, folic acid, Hb, Ht, MCV in LHON patients and controls
- if an vitamin B12 deficiency is detected, a referral to inernal medicine will follow for evaluation of the cause of deficiency

Study burden and risks

The burden of the participants is a single blood examination (venapunction)

Contacts

Public
Universitair Medisch Centrum Groningen

Postbus 30.001
9700 RB Groningen
NL
Scientific
Universitair Medisch Centrum Groningen

Postbus 30.001
9700 RB Groningen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

LHON patients:
-clinical characteristics of LHON
-proven LHON mutation
- recent loss of vision (not longer then half a year);Control patients:
- same gender as LHON patient for which will be matched
- same age (+/- 3 years) as LHON patient for which will be matched (but not younger then 18 years)

Exclusion criteria

LHON patient
- younger then 18 years;Control patients
-known optic neuropathy
-actual treatment by medical specialist (except ophthalmologist)
- known bowel disease, for which patient receives treatment
- actual neurological disease, for which patient is under treatment
- known renal dysfunction
- known diabetes mellitus
- known thyroid disease
- known anemia
- veganistic diet
- excess alcohol intake (> 4 units a day)
-pregnancy
- medication: gastric acid secretion inhibitors, colchicine
- smoking

Study design

Design

Study type: Observational invasive

Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-06-2012
Enrollment:	72
Type:	Actual

Ethics review

Approved WMO

Date:	28-10-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL36739.042.11