Investigation of cerebrovenous haemodynamics by transcranial and extracranial Color-Doppler sonography and MR-venography in patients with multiple sclerosis and healthy controls.

Published: 18-01-2011
Last updated: 04-05-2024

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

Summary

ID

NL-OMON36557

Source
ToetsingOnline

Brief title
Cerebral venous drainage in MS patients and controls

Condition

- Demyelinating disorders

Synonym
inflammatory disease of the central nervous system, multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Elisabeth Ziekenhuis
Source(s) of monetary or material Support: nationaal MS fonds

Intervention

Keyword: cerebral venous drainage, multiple sclerosis, prevalence

Outcome measures

Primary outcome

Presence of two or more of the five parameters of impaired cerebral venous

drainage as seen in chronic cerebrospinal venous insufficiency in MS patients

and healthy controls is the main study parameter.

Secondary outcome

Secondary parameters: prevalence of chronic cerebrospinal venous insufficiency

in MS patients and healthy controls.

Study description

Background summary

Background:
The sequence of events underlying the development of the inflammatory plaques in multiple sclerosis (MS) remains still unclear. MR-studies show plaques in MS are venocentric, MS progresses along the venous vasculature. Histological studies of plaques in MS reveal aspects of any status of chronic cerebrospinal venous insufficiency (CCSVI) such as the perivascular fibrin cuffs of infiltrating cells and the peculiar disposition of perivenous iron stores. It is known that chronic impaired venous drainage in lower extremities leads to increased iron stores in affected tissue and chronic infections with poor skin healing. Clinical investigators have become increasingly aware of the parallels between iron-dependent inflammation in impaired venous drainage of the lower extremities and iron deposits near inflammatory areas in MS.
Prevalence estimates of CCSVI in MS range widely. A few studies have attempted to identify this prevalence in MS patients and healthy controls, with contradictory results. The prevalence of CCSVI in MS and the association with

its pathogenesis is still unclear.

Also the best technique to assess impaired venous drainage is open for discussion. Zamboni et al, the group who detected CCSVI, used transcranial and extracranial Color-Doppler sonography. A recent study by the investigators at the free University of Amsterdam using magnetic resonance venography (MRV) did not show a significant increased incidence of CCSVI in 20 patients with MS. However, a recent study at the Buffalo University, USA, showed that Color Doppler sonography at the moment is the best technique to assess impaired venous drainage and that MRV is not suitable to assess CCSVI.

The recent findings of CCVSI in MS and its enormous global impact on the care for MS patients resulting in unproven treatment of CCSVI with its possible risks are reasons to perform a study amongst a large group of Dutch patients with MS and in healthy subjects to assess the prevalence of CCVSI in these groups.

Hypothesis:
1. CCSVI in MS patients occurs more frequently in comparison to healthy controls
2. CCSVI is more common in MS patients with a longer disease duration of MS
3. CCSVI is more common in MS patients with a progressive clinical course
4. The pattern of CCSVI in the primary progressive course, characterized by MRI demonstration of MS plaques in the spinal cord, is in particular stenosis of the azygous vein
5. The use of MRV for diagnosis of CCSVI in MS patients has limited value

Study objective

The primary objective of this study is to determine the prevalence and degree of impaired cerebral venous drainage in MS patients in comparison to healthy subjects.

Secondly, we want to determine a possible relationship between the degree of impaired cerebral venous drainage and signs of peripheral impaired venous flow, the haemosiderinuria concentration and serum concentration of soluble transferrin receptor and serum ferritin levels.

The third objective is to determine a possible relationship between age, gender, clinical type of the disease, disease progression, and the presence of impaired cerebral venous drainage.

Study design

Observational study

Study burden and risks

Burden:
One visit to the hospital, one phsyical examination.
One urine sample and one blood sample of 2 ml, for 40 MS patients and 40 healthy controls.
For twenty MS patients intravenous contrast will be given undergoing the MR-venography.

Risks:
There are no risks associated with participation.

Benefit:
We hope to improve understanding the pathogenesis of the MS plaques by investigating cerebral venous drainiage as a possible mechanism related to increased iron deposition in MS plaques.

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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

a. Patients affected by clinical defined MS, diagnosed according to the McDonald criteria. Relapsing-remitting MS, secondary-progressive MS, primary-progressive MS.
b. Age > 18 years and less than 65 years.

Exclusion criteria

a. We exclude from the study those subjects having, or showing the potential for developing, a
nervous system pathology of a venous refluxive and/or obstructive nature, including:;1. Chronic venous insufficiency of the lower limbs
2. History of venous thrombosis and/or post-thrombotic syndrome
3. Genetic thrombophilia
4. Congenital angiodysplasias
5. Congenital vascular malformations
6. Budd-Chiari syndrome
7. Behcet disease
8. Other vasculitis;b. An acute relapse and/or steroid treatment within the 30 days preceding study entry
c. CIS patients (clinically isolated symptoms), that is patients with the first episode fitting with central demyelination.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-01-2011
Enrollment:	220
Type:	Actual

Ethics review

Approved WMO

Date:	18-01-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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	NL33659.008.10