The significance of biomarkers in the blood in the diagnosis and the course of Alzheimer*s disease

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Dementia and amnestic conditions
Study type	Observational invasive

Summary

ID

NL-OMON34678

Source
ToetsingOnline

Brief title
Blood biomarkers for Alzheimer*s disease

Condition

- Dementia and amnestic conditions

Synonym
Alzheimer□s disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Eigen ziekenhuis;GGZ Noord en Midden Limburg

Intervention

Keyword: - Alzheimer□s disease, - Blood biomarkers

Outcome measures

Primary outcome

- Descriptives (gender, age, education level, demographics)

- Biochemical biomarkers: neopterin, total amino acid spectrum, HVA, BDNF and

S-100B

- Comorbidity (CIRS-G)

- Drug use

- MMSE score, neuropsychological examination and MRI cerebrum

- The Clinical Dementia Rating (CDR) scale

- Evolution: intercurrent diseases

Secondary outcome

nvt

Study description

Background summary

In previous studies, Neopterin plasma concentrations, a marker of cell-mediated immune activation and
inflammation, were found to be higher in AD patients as compared to the healthy age-matched controls
(Leblhuber et al, 1999; Hull et al, 2000). Blasko et al (2007) have found a correlation between neopterin
concentrations and the cognitive decline in patients with AD. Also in patients with Down syndrome (DS) the
value of neopterin in the blood showed to be significantly increased in DS patients with AD compared to DS
patients without AD (Coppus et al, 2009). A follow-up study of DS patients showed that the concentrations of

nearly all amino acids in DS subjects with AD differed significantly from those of healthy controls, the production
of Nitric Oxide (NO) related amino acids as reflected by an increased citrulline/arginine ratio (Cit/Arg ratio) was
enhanced during development of clinical dementia and this correlated to Neopterin plasmaconcentrations.
Furthermore, it was found that neurotrophic proteins play a crucial role in cognition, learning and memory formation
because they modulate synaptic plasticity. The neurotrophic protein Brain-derived neurotrophic factor (BDNF) plays
an important role in the changes of cognition and plasticity witch found in AD (Hubka et al, 2006). The neurotrophic
protein S-100B is involved in degeneration of the central nervous system in AD.

Study objective

The research aims to answer the following questions:

- Are the concentrations of neopterin, amino acids, HVA, S-100B and BDNF in the blood of patients with Alzheimer's
disease differ from those in a matched healthy controls group (matched for age, sex, education and comorbidity).

- What is the diagnostic value (sensitivity, specificity, positive predictive value) of these biomarkers and combinations
of these biomarkers for AD diagnosis?

- Do the AD biomarker values similar to those of AD in Down syndrome patients or they are different?

Study design

In 50 patients diagnosed with "probable Alzheimer's" (AD), according to the NINCDS-ADRDA criteria
(CBO guideline Dementia), and in 50 healthy subjects (matched on age, sex, education and comorbidity),
blood samples will be taken in VieCuri Medical Center in Venlo to determine the following biomarkers
concentration: neopterin, total amino acid spectrum, HVA, BDNF and S-100B. In the healthy control group
MMSE is required before the blood test to detect the cognitive state.

Study burden and risks

The risk of complications related to venipuncture are negligible

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

Patient inclusion criteria:
- Patients with Alzheimer's disease
- Mentally competent AD patient [Clinical Dementia Rating (CDR) scale 1]
- The diagnosis of "probable Alzheimer's disease* should be made according to the NINCDS-ADRDA criteria.
- Patients or carers should agree with the study (written informed consent is required form patients or their carers).;Inclusion criteria control group (healthy subjects in group A):
- Men or women without cognitive or psychiatric disorders
- Mini-Mental State Examination (MMSE) score >= 28

Exclusion criteria

Patient exclusion criteria:
- Mentally incompetent AD patient [Clinical Dementia Rating (CDR) scale 2 and 3]
- Patients with infection or inflammatory disease less than 1 months ago.
- Patients with active malignancy.
- Patients with autoimmune disease (e.g. temporal arteritis, polymyalgia rheumatica).
- Patients who use immune modulating drugs (e.g. Immunocyanin, interferon gamma, immunoglobulin).
- Patients with renal dysfunction (MDRD <50)
- Patients with liver impairment
- Patients with decreased serum albumin <25 g / l;Exclusion criteria control group:
- Conform the patient exclusion criteria

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-01-2011
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	22-10-2010

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL31507.091.10