Effect of repeated intranasal cobalamin (Vitamin B12) administration on cobalamin deficiency in elderly

Published: 23-12-2013
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The objective of this study is to establish the optimal intranasal cobalamin dosing regimen in elderly.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vitamin related disorders
Study type	Interventional

Summary

ID

NL-OMON45137

Source
ToetsingOnline

Brief title
ERICA

Condition

- Vitamin related disorders

Synonym
Vitamin B12 deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Kennemer Gasthuis
Source(s) of monetary or material Support: Eigen financiering (Apotheek;Universiteit Utrecht)

Intervention

Keyword: cobalamin, deficiency, elderly, intranasal

Outcome measures

Primary outcome

Change in total transcobalamin and holotranscobalamin (holoTC)

serumconcentrations over time.

Secondary outcome

Change in methylmalonic acid (MMA) and homocysteïne (tHcy) serum concentrations

and change in Geriatric Depression Scale (GDS) 5 and Mini Mental State

Examination (MMSE) score over time.

Study description

Background summary

Among elderly the prevalence of cobalamin (Vitamin B12) deficiency is estimated to be between 10 and 50%, with the highest rates in the geriatric population. Cobalamin is a cobalt containing vitamin that serves as a coenzyme for several important biochemical reactions in the formation of blood and the functioning of the brain and nervous system. Consequently, cobalamin deficiency causes anaemia and irreversible neurological damage.
In the acidic environment in the stomach, cobalamin is extracted from food proteins by pepsin. Subsequently, cobalamin is bound to the intrinsic factor in the duodenum and actively absorbed in the intestines. Hence, lack of intrinsic factor and changes in gastric physiology due to aging or use of certain drugs (i.e. proton pump inhibitors, metformin) impair cobalamin absorption and cause cobalamin deficiency.
The standard treatment for cobalamin deficiency is administration of cobalamin by way of intramuscular injection. These injections, however, have several disadvantages. Injections are painful, injection related adverse events such as infections and bruises may occur and these injections cannot be self-administered by the patients. Safer and more convenient ways of administration such as oral and intranasal administration are therefore being explored. Oral treatment, however, is not an option in patients that are unable or unwilling to take oral medication. Intranasal administration of cobalamin

seems a suitable alternative for both cobalamin injections and oral administration in elderly.
Reproducible intranasal cobalamin absorption has been demonstrated in healthy elderly volunteers en patients with ileal resections. These studies, however did not provide insight in the pharmacokinetics of intranasal administered cobalamin compared to intramuscular administered cobalamin in elderly. Therefore we previously we explored the pharmacokinetics of intranasal administered cobalamin compared to intramuscular administered cobalamin in cobalamin deficient elderly. This study demonstrated significant differences in the pharmacokinetics between cobalamin administered by intramuscular injection and cobalamin administered by intranasal spray. Despite these differences, intranasal administration of a single dose of 1000 microgram cobalamin led to a cobalamin serum level well within the therapeutic cobalamin range (preliminary data). The maximum cobalamin serum level of 1000 pmol/l found is this study is comparable to the maximum cobalamin serum level after an oral dose of 1000 microgram cobalamin. As mentioned above, daily oral cobalamin administration has been shown effective in treating cobalamin deficiency. Hence, the absorption of intranasal administered cobalamin seems sufficient to effectively treat cobalamin deficiency. Although this study provided insight in the pharmacokinetics of intranasally administered cobalamin it, however, did not provide insight in the optimum intranasal dosage regimen for treating cobalamin deficiency.
In order to establish an optimum dosage regimen for intranasal cobalamin administration in cobalamin deficient elderly the effects of two intranasal cobalamin 1000 microgram dosage regimens i.e. once every three days and once every day, followed by once every week are evaluated in this study.

Study objective

The objective of this study is to establish the optimal intranasal cobalamin dosing regimen in elderly.

Study design

A randomized, open, comparative intervention study.

Intervention

Randomisation; patients will be randomised over two intranasal dosage regimens.

Arm A:
1000 microgam every day for two weeks, followed by 1000 microgram once every week for three months (90 days).

Arm B:

1000 microgram every three days for three months (90 days)

Study burden and risks

Per subject a total of 6 blood samples are collected to assess cobalamin, methylmalonicacic and homocystein serum levels over time.
Subjects have to come to the hospital twice; at the beginning and at the end of the sudy. The first and last blood samples will be taken at the geriatric departmen.
Both dosageregimens will raise cobalamin serum levels. Cobalamin serum levels in the once every 3 days administration group might not be raised to the same extent as in the once every day administration group. Normalization of serum cobalamin levels might therefore, take longer in subjects in the once every 3 days administration group.
A cobalamin dose of 1000 µg was chosen because this corresponds with the registered cobalamin intramuscular injection dose.
After participating in this study subjects are transferred to standard care and treatment for cobalamin deficiency or if maintenance therapy is nescessary.

Contacts

Public
Kennemer Gasthuis

Boerhaavelaan 24
Haarlem 2035RC
NL
Scientific
Kennemer Gasthuis

Boerhaavelaan 24
Haarlem 2035RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

65 years of age or over,
Cobalaminconcentration less than 250 pmol/l,
Suspect for cobalamin deficiency; hyperhomocysteinemia (> 15 micromol/l) and/or 2 or more symptoms of cobalamin deficiency e.g. fatigue, memory impairment, irritability, personality changes, muscle weakness, depression, poor appetite, weight loss
Capable of understanding the study informaton
Informed consent

Exclusion criteria

Concomitant use of intranasally administered medication,
Chronic rhinitis,
Use of cobalamin containing dietary supplements,
Severe Renal impairment i.e. MDRD less than 20 ml/min,
MMSE score < 19

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-06-2014
Enrollment:	60

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	Vitamin B12 nasal spray

Ethics review

Approved WMO Date:	23-12-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2013-000356-18-NL
CCMO	NL43211.094.13

Study results

Date completed:	17-03-2022
Actual enrolment:	60