Effect of administration route on the pharmacokinetics of cobalamin in elderly

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Establishing the pharmacokinetics of intranasally and intramuscularly administered cobalamin in elderly.

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

Summary

ID

NL-OMON36589

Source
ToetsingOnline

Brief title
Pharmacokinetics of Cobalamin

Condition

- Vitamin related disorders

Synonym
Cobalamin deficiency or Vitamin B12 deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Apotheek der Haarlemse Ziekenhuizen
Source(s) of monetary or material Support: Stichting Apotheek der Haarlemse Ziekenhuizen

Intervention

Keyword: administration route, cobalamin, elderly people, pharmacokinetics

Outcome measures

Primary outcome

The AUC48hours of intramuscular compared with intranasal administration.

Secondary outcome

Not applicable

Study description

Background summary

Approximately 10-15% of the population aged 65 years and older has cobalamin (Vitamin B12) deficiency. An even higher prevalence of 30-40% is reported for malnourished and sick elderly people. Cobalamin serves as a cofactor for several vital biochemical reactions. If deficient, people may suffer from anaemia, irreversible neurological damage resulting in cognitive impairment, and neuropsychiatric disorders. Cobalamin deficiency is due to malabsorption of food-bound cobalamin or insufficient dietary intake.
Administration of cobalamin by way of intramuscular injection is the gold standard for cobalamin deficiency treatment. It, however, has several disadvantages. Injections are painful, injection related adverse reactions may occur, and health care professionals are usually needed to administer these injections. The latter increases the costs of the treatment considerably. A more convenient, safer and cost-effective treatment would, therefore, be advantageous to both patients and the health care system in general.
Food-bound cobalamin is actively absorbed. In contrast, crystalline cyanocobalamin administered in capsules is absorbed by way of passive diffusion although at a relatively low efficiency. Approximately 1% of an oral dose of crystalline cyanocobalamin is absorbed. Oral administration of cyanocobalamin is, however, efficacious in normalising serum cobalamin levels.
Oral treatment is not an option in patients that are unable to take oral medication or patients with severe diarrhoea or vomiting. Dysphagia is a common condition in the elderly population due to age related pathologic changes or due to cerebrovascular diseases affecting the swallowing mechanism. Intranasal administration of cobalamin seems a suitable alternative for both cobalamin injections and oral administration in elderly.
The absorption of intranasal administered cobalamin was demonstrated in two

studies. In these studies, intranasal administration of cobalamin has not been compared to intramuscular administered cobalamin. Insight in the pharmacokinetics of intranasal administered cobalamin in comparison with intramuscular injection is, however, required to determine the optimal dosage regimen. In addition, the absorption of intranasal administered cobalamin has been examined in healthy elderly volunteers and patients with ileal resections or Crohn*s disease only, though cobalamin deficiency is more prevalent in the sick and/or malnourished elderly population.
In order to determine a dosage regimen for intranasal administered cobalamin in elderly patients insight in the pharmacokinetics of intranasal administration compared to intramuscular administration of cobalamin has to be obtained. Because there are no published pharmacokinetic data of intramuscular cobalamin in elderly patients both routes of administration need to be investigated.
In this study we investigate the effects of two routes of administration i.e. cobalamin administered intranasally and cobalamin administered by intramuscular injection on the pharmacokinetics as expressed in the standard parameters AUC48hours, Cmax, Tmax and T1/2 in eldery patients.

Study objective

Establishing the pharmacokinetics of intranasally and intramuscularly administered cobalamin in elderly.

Study design

A randomized, open, comparative, intervention study.

Intervention

Randomsation, first cobalamin dose can be administered by the standard intramuscular injection or by intranasal spray.

Study burden and risks

Per subject a total of 10 blood samples are collected to assess cobalamin levels over time. This information is used to calculate the AUC48 hours. All subjects will be given a peripheral venous catheter (*venflon*) to make the collection of blood samples less invasive.
Both routes of administration will raise cobalamin serum levels. Cobalamin serum levels in the intranasal administration group might not be raised to the same extent as the cobalamin serum levels in the intramuscular administration group. Normalization of serum cobalamin levels might therefore, take longer in subjects in the intranasal administration group.
After participating in this study subjects are transferred to standard care and treatment for cobalamin deficiency.

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

- Cobalamin deficiency (cobalamin serum level less than 200 pmol/l)
- Age 65 years or over
- Capable of understanding the study information
- informed consent

Exclusion criteria

- Concomitant use of nasally administered medication
- Chronic rhinitis
- Running nose
- Clinical relevant infection

- Hemodynamic Instability
- Short Nutritional Questionnaire Score (SNAQ) of 3 or over
- Use of cobalamin containing dietary supplements
- Severe Renal impairment i.e. MDRD less than 20 ml/min
- Ethical or medical reasons upon discretion of the investigators

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):	01-09-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Hydrocobamin
Generic name:	Hydroxocobalamin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Nascobal intranasal spray
Generic name:	cyanocobalamin intranasal spray

Ethics review

Approved WMO

Date:	28-04-2011

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2011
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

ID: 20477
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2011-001542-15-NL
CCMO	NL33450.029.11
OMON	NL-OMON20477