Vitamin D and non-specific musculoskeletal complaints in non-Western immigrants

Published: 13-11-2013
Last updated: 22-04-2024

We aim to assess the effect of high-dose vitamin D supplementation on non-specific musculoskeletal complaints in non-Western vitamin D-deficient immigrants and to determine whether improvement of mood is associated with this effect.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Musculoskeletal and connective tissue disorders NEC
Study type	Interventional

Summary

ID

NL-OMON40574

Source
ToetsingOnline

Brief title
Vitamin D and musculoskeletal complaints in non-Western immigrants

Condition

- Musculoskeletal and connective tissue disorders NEC
- Mood disorders and disturbances NEC

Synonym
muscle pain, non-specific musculoskeletal complaints

Research involving
Human

Sponsors and support

Primary sponsor: Huisartsenpraktijk Handellaan
Source(s) of monetary or material Support: eigen geld van onderzoeker. Sponsoring

wordt nog gezocht. Medicatie wordt wsl gratis geleverd door Merck KGaA

Intervention

Keyword: ethniciy, general practice, musculoskeletal disease, vitamin D

Outcome measures

Primary outcome

Our primary goal is to assess the difference in self-reported improvement of

pain 12 weeks after administration of placebo or 2x 200.000 IU cholecalciferol

.

Secondary outcome

Secondary outcome measures will be: self-reported improvement of pain in 6

weeks, (improvement of) mood and fatigue at week six 6 and week 12 and

correlation of these improvements with eachother and with the level of 25-OH-D

and with bio-available vitamin D at start. Also we will assess improvement in

ability to walk stairs at week six and week 12 and correlation with pain in the

legs and fatigue at baseline

Correlation of VAS-scores for pain with self-reported pain will be assessed

too.

Study description

Background summary

Several investigators found an association between low serum-vitamin D levels and musculoskeletal complaints (Plotnikoff 2003, Erkal 2006, Mouyis 2008) and muscle strength (Glerup 2000, Biss-Ferr 2004, Ward 2009), though others did not (Helliwell 2006, Reed 2007). Anyhow, many observational studies (case-reports as well as intervention studies) report a beneficial effect of vitamin D supplementation on musculoskeletal diseases or complaints. Some reported this

in one to six weeks, (Gloth, 91 Prabhala ,00 Badsha 09 Grootjan 02) but longer intervals are reported too (de la Torrente 04, Nellen 96 Glerup 00, Al Farraj 03). Moreover, vitamin D supplementation proved to enhance muscle strength (Glerup 00,Dhesi 04, Bishoff-Ferrari 04 ,Lips 10,Ward 10). In a systematic review Straube could find no proof for a positive effect on musculoskeletal complaints of this therapy. (Straube / Cochrane2010).
After this review three randomized controlled trials (RCT) on this subject were published: one did not prove pain-relieving effect of vitamin D3 (2 x 10E5 IU or 800 IU/d) in six months in vitamin D-deficient non-Western immigrants (18-65yr). However, this study was not designed to evaluate pain-modifying effect of vitamin D (Wicherts, 2010). Another was done in Turkish elderly, who did not get relief from 300.000 IU vitamin D3 in 4 weeks. (Sakalli, 2011). The third one was done by our group: 84 non-western immigrants, included with low 25-OH-D levels and > 3 months pain, were successfully treated for 6 weeks with 150.000 IU; a better effect after 12 weeks was suggested (Schreuder 2012).
A direct effect of vitamin D on muscle cells has pathological ground: muscle cells have *like many other tissues- vitamin D receptors (Simpson 1985, Bischoff, 2001 Ceglia 2008). Also enhancement of mood as an indirect effect on complaints could be an explanationIn a systematic review and meta-analysis (Anglin, 2013) an association of depression and low 25-OH-D levels was found in 10 cross-sectional studies, but also in 3 cohort-studies in the elderly: people with 25-OH-D > 75 nmol/L were less prone to develop depression, though an effect of having levels < 50 nmol/L could not reliably determined in that study. Three intervention-studies for depression were published only after this analysis: after 6 months of supplementation (40.000 IU/wk) no improvement of depressive symptoms was found in a RCT in healthy volunteers, whether with high or low 25-OH-D levels (Kjaergard, 2012). In a second RCT in 40 patients with depression fluoxetine with 1500 IU/d vitamin D had better effect on depression than fluoxetine only (Khoraminya, 2012). In a third (not blinded) trial in depressed patients with low levels of 25-OH-D got 150.000 IU or 300.000 IU vitamin D or placebo. After three months the treated groups improved 5 resp, 7 points on the Beck Depression Index (Mozzafari, 2013) Non-Western immigrants in Western Europe are prone to vitamin D deficiency (Shaunak 1985, Bergman 2001, Erkal 2006, Wielders 2006, Hirani 2009) and also more often have musculoskeletal problems than Caucasian people (Bergman 2001, Allison 2002, Mc Farlaine 2005). Also bad mood is 1,5x more prevalent in non-Western immigrants in the Netherlands (www.statline.cbs.nl). Because bad mood and having physical complaints are strongly correlated improvement of mood could be a cause as well a result of improvement of aspecific musculoskeletal complaints.

Study objective

We aim to assess the effect of high-dose vitamin D supplementation on non-specific musculoskeletal complaints in non-Western vitamin D-deficient immigrants and to determine whether improvement of mood is associated with this effect.

Study design

Double blinded randomised controlled trial

Flow Diagram:

NW immigrants suffering > 3mnd non-spec
musculoskel. complaints, 25-OH-D <50nmol/L

Wk 0 Informed consent, Base-line metingen bij POH
+ Randomisation

200.000 IE vit D3 placebo

Wk 6 questionnaire questionnaire
200.000 IE vit D3 placebo

Wk 12 questionnaire questionnaire
evt 25-OH-D evt 25-OH-D

Intervention

One group gets 200.000 IU vit D3 at week 0 and week 6
The other group get placebo at week 0 and week 6 and after de-blinding 200.000 IU vit D3 at week 12

Study burden and risks

About risk:
Adverse effects of 400.000 IU vitamin D3 administered in 6 weeks are almost non-existent. Treatment of osteomalacia or rachitis is done with (in 6 weeks cumulative) doses of 2.000.000 IU. Studies showed that 25-OH-D levels less than 500 nmol/L are harmless (R.Vieth 2006). Because every 400 IU/day raises 25-OH-D levels ca 10 nmol/L the dose used in this study can raise levels only 175 nmol/L. In my former trial, in which the same doses were used, nobody got levels above the 125 nmol/L (Schreuder, 2012) The patient in this study (included with levels < 50 nmol/L) will stay far under the 500 nmol/L level, even when they dicide to use extra vitamin D themselves.
A supplementationtrial in the UK investigating supplementation with 200.000 IU viutamin D in one gift showed no adverse effects (Daksha, 2003)
So, in case of sudden unexpected complaints first other causes should be examined. If needed the given dose vitamin D can be known by contacting the

investigator; also a 25-OH-D level and calciumlevel can be easily determined. Because vitamin D is a well-knwon drug that has been used for many years its very unlikely new, unknown adverse effects wil be found.

About burden:
For diagnosis and treatment for non-specific musculoskeletal pain the GP will advice a bloodproof anyhow. Beside the 25-OH-D the patient will get his kreatinine investigated also for the sake of this study: a very small burden in my opinion.
Patient will complete 4 times a questionnaire and will have an informed consent procedure. This will take ca 75 min of his time; traveling and waiting times comes extra.

About benifit:
Often bad mood or depression is underdiagnosed by GP's as well as by the patients themselves. The nature of the questionnaires and the contact with the POH-GGZ facilitates recognition and treatment of this mood-disorders (if they exists)
Many supplemented patient are curious to know their 25-OH-D level after supplementation. They will get the opportunity to know (if they want to)

Contacts

Public
Huisartsenpraktijk Handellaan

Handellaan 108-D
Delft 2625 SN
NL
Scientific
Huisartsenpraktijk Handellaan

Handellaan 108-D
Delft 2625 SN
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

non-Western immigrants, 18-60 yr, not pregnant
non-specific musculoskeletal complaints (<= all musculoskeletal complaints without obvious cause (e.g. trauma, R.A.) or well-defined symptomatology or localisation (e.g. gonarthrosis, HNP) "diagnosis" like low back pain, cervico-brachial syndrome or fasciitis plantaris etc. are included. Depression is NOT an exclusion-criterium)
a. lasting > 12 wks
or b. 3 period (or more) of pain >1 month in 2 yr
25-OH-D < 50nmol/L

Exclusion criteria

Pregnancy
Supplementation with vitamin D in the last 4 months
Rachitis, Osteomalacia, Sarcoidose, ESR>35, kreatinine > 150 mmol/L, Calcium > 2,55 mmol/L
Use of Statines, Corticosteroids or Cyclosporin

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	200
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Vigantol oil
Generic name:	cholecalciferol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	13-11-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-12-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	28-02-2014
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	02-05-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2013-002928-16-NL
ISRCTN	ISRCTN70909899
CCMO	NL45457.098.13