A Prospective, randomized , placebo, controlled trial (double blinded) to assess the potential role of vitamin D treatment in breast cancer patients

Published: 24-11-2010
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To assess impact of high doses vitamin D on tumour histology in breast cancer patients

Ethical review	Not approved
Status	Will not start
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON34378

Source
ToetsingOnline

Brief title
Potential role of Vitamin D treatment in Breast Cancer

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer/ breast carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Spectrum Twente
Source(s) of monetary or material Support: Eli Lilly,Procter & Gamble,stichting Coronis;onderzoeksstichting van de maatschap gynaecologie Enschede

Intervention

Keyword: apoptosis, breast cancer, proliferation, vitamin D

Outcome measures

Primary outcome

1. To study the influence of vitamin D on immunohistochemical marker Ki 67 (proliferation marker) in breast cancer. This marker will be defined in the biopsy specimen and in the tumour resection specimen. The mean difference between these two marker values will be examined between the intervention and the control group.

Secondary outcome

1. To study the influence of vitamin D on immunohistochemical markers in biopsy specimen and tumour resection specimen in breast cancer. These markers will be defined in the biopsy specimen and in the tumour resection specimen.

o Immunohistochemical markers to be studied are

* Caspase 3 (apoptosis marker)

* Vitamin D receptors (responsiveness marker)

* HER 2Neu-, estrogen- and progesterone-receptor status (tumormarkers)

2. To study changes in serum calcium and vitamin D levels between day 1 and day of surgery

3. Correlation of initial (=before treatment with vitamin D) serum vitamin D levels with clinicopathological parameters of breast cancer (tumour size, nodal status, grade, estrogen and progesterone receptor status, HER2 status).

4. Reporting any eventual adverse effects.

Study description

Background summary

1. INTRODUCTION AND RATIONALE
Although the exact relationship between vitamin D and (breast) cancer remains unclear, a growing body of evidence suggests vitamin D could account for several favourable effects on (breast) cancer prognosis and tumour biology (1, 2).

Previously, data from epidemiological studies were inconclusive about the effects of vitamin D and the risk of breast cancer. A recent meta-analysis of Chen et al however, provides strong evidence for a chemopreventive effect of vitamin D against breast cancer (3). Combining the results of 11 studies that examined the relationship between vitamin D intake and breast cancer risk, a significant decrease in breast cancer risk was found for those with highest quantile of vitamin D intake compared with the lowest intake (RR=0.55, 95% CI = 0.85-0.97) (3). They also reported a significant inverse relationship between serum 25(OH) vitamin D levels and breast cancer risk (3). However, there are no large, prospective, randomized controlled trials administering high doses of vitamin D to investigate effects on breast cancer risk or histology (2, 3). The rationale is to perform such a study.

The suggestive chemopreventive effect of vitamin D is biological plausible (2). Many tissues, including breast tissue, express 1, 25 vitamin D hydroxylase and are thus able to convert the predominant inactive and circulating 25(OH) vitamin D to its active 1, 25(di-OH) metabolite. This active metabolite can bind the vitamin D receptor, present in nuclei of most cells, to form a nuclear transcription factor regulating cell differentiation, proliferation and apoptosis (4). This has been confirmed both in in vivo (animal experiments) and in vitro experiments (1, 3, 5). Therefore, the rationale is to investigate proliferation and apoptosis markers in this study.

Vitamin D is readily available, relatively safe and cheap. Breast cancer is the most frequent malignancy in women in the Netherlands (6). Therefore, this study could have a major impact on breast cancer management if beneficial effects of vitamin D supplementation on breast cancer histology could be demonstrated. There are currently no studies addressing this question in breast cancer patients, however, we found one study currently recruiting male patients to address this question in prostate cancer patients (7).

An published review about vitamin D administration in Multiple Sclerosis patients confirmed the safety of vitamin D (11). In this trial patients consuming progressively rising amounts of cholecalciferol, ending with one month of intake at 40,000 IU/day exhibited no detectable effect on serum

calcium concentration or urinary calcium excretion. Furthermore, the published literature contains no cases of vitamin D intoxication at long-term doses up to 40,000 IU/day (8). For these reasons, we have chosen to use 40,000 IU/day as a maximum dose for a period up to 8 weeks.

Study objective

To assess impact of high doses vitamin D on tumour histology in breast cancer patients

Study design

prospective Randomized controlled trial

Intervention

Intervention:
1. Vitamin D supplementation, 40.000 IU/day in the intervention group and placebo in the control group, both 55 patients each. Supplementation starts after breast cancer diagnosis is communicated with the patient and will be continued until surgery is performed (estimated window of treatment = 3-8 weeks).
2. Blood samples will be taken at time of diagnosis and every 14 days until day of surgery and at day of surgery

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
1. daily intake of Vitamin D (orally) (burden)
2. two-weekly extra blood samples and at day of diagnosis and at day of surgery (burden)
3. the potential and biological plausible positive effects on primary tumour and circulating tumour cells (benefit).

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

primary operable invasive breast cancer

Exclusion criteria

Previously clinically detected nefrolithiasis (on diagnostic imaging techniques).
Previously clinically detected cholelithiasis (on diagnostic imaging techniques).
History of sarcoidosis.
History of recurrent urolithiasis.
Already taking Vitamin D (colecalciferol) supplement >400 IU/day.
Calcium-lowering therapy within 2 weeks before study entry.
Previously documented impaired renal function.

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:	110
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	colecalciferol
Generic name:	colecalciferol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	24-11-2010
Application type:	First submission
Review commission:	METC Medisch Spectrum Twente (Enschede)

Not approved

Date:	14-02-2011
Application type:	First submission
Review commission:	METC Twente (Enschede)

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: 28013
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2010-019868-37-NL
ClinicalTrials.gov	NCTnummerisaangevraagd
CCMO	NL33552.044.10
OMON	NL-OMON28013